

TEAT

CEPERLEY 09/647,518

Considered  
12/08/01

=> d his

(FILE 'HOME' ENTERED AT 16:23:16 ON 16 AUG 2001)

FILE 'HCAPLUS' ENTERED AT 16:23:25 ON 16 AUG 2001

L1 25 S FRIEDE M?/AU  
L2 19 S HERMAND P?/AU  
L3 39 S L1-2  
L4 16 S L3 AND ADJUVANT  
L5 3 S L4 AND POLYOXY?  
SELECT RN L5 1-3

INVENTOR SEARCH

FILE 'REGISTRY' ENTERED AT 16:25:09 ON 16 AUG 2001

L6 29 S E1-29

FILE 'HCAPLUS' ENTERED AT 16:25:20 ON 16 AUG 2001

L7 3 S L5 AND L6

3 cites w/ 29 compounds displayed

FILE 'REGISTRY' ENTERED AT 16:28:42 ON 16 AUG 2001

L8 14 S L6 AND PMS/CI  
L9 15 S L6 NOT L8  
L10 3 S L9 AND "NONA"  
L11 1 S L9 AND "TETRA"  
L12 4 S L10-11  
L13 11 S L9 NOT L12  
L14 1 S L13 AND "OCTA"  
L15 5 S L12 OR L14  
L16 207440 S PETH/PCT  
L17 154158 S PES/PCT

14 cpds from inventor that are polyoxy polymers

5 cpds fr. inventor that are polyoxy cpds

FILE 'HCAPLUS' ENTERED AT 16:33:12 ON 16 AUG 2001

L18 108766 S L8  
L19 568 S L15  
L20 9892 S L18(L)THU/RL  
L21 26016 S ADJUVANT  
L22 48314 S VACCIN?  
L23 73 S L20(L)L21  
L24 416391 S AQUEOUS(3A)SOLUTION  
L25 51337 S MICEL?  
L26 5 S L23 AND L24-25  
L27 5 S L26 NOT L7  
L28 28271 S LT OR CT OR 3D-MPL OR CPG OR QS21  
L29 1 S L28 AND L27  
L30 4 S L27 NOT L29  
L31 5 S L23 AND L28  
L32 4 S L31 NOT L27  
L33 3 S L32 NOT L7  
L34 250 S L18(L)L21  
L35 16 S L34 AND L24-25  
L36 1 S L35 AND L28  
L37 13 S L35 NOT EMULS?  
L38 10 S L37 NOT (L7 OR L36 OR L27 OR L28)  
L39 388311 S ?ACRYLAT? OR ?ACRYLIC  
L40 10 S L38 NOT L39  
L41 81791 S VESIC?  
L42 10 S L40 NOT L41  
L43 36342 S POLYOXYETHYLEN?  
L44 144 S L43(L)L21-22  
L45 13 S L44 AND L24-25  
L46 2 S L28 AND L44  
L47 0 S L45 AND L46  
L48 13 S L45-46 NOT (L7 OR L36 OR L27 OR L28 OR L42)

searching applicants cpds

1 cite  
4 cite

3 cites

1 cite

10 cites

13 cites

Ceperley, Mary

12/08/01

T : STIC-ILL  
Subject: REF. ORDER FOR 09/647,518

PLEASE PROVIDE ME WITH A COPY OF EACH OF THE FOLLOWING REFERENCES. THANKS.

RINELLA ET AL  
J. COLLOID INTERFACE SCI. (1998) 197(1), 48-56.

TEERLINK ET AL  
VACCINE(1987) 5(4), 307-314.

SINGH ET AL  
J. AM. OIL CHEM. SOC. (1984), 61(3), 596-600.

NAKANISHI ET AL  
CHEM. PHARM. BULL (1983), 31(11), 4161-4166.

ULLMAN ET AL  
ARCH. PHARM. (WEINHEIM , GER.) (1972) 305(11), 797-802.

KOROSSYOVA ET AL  
PHARMAZIE (1971), 26(11), 682-685.

TODD ET AL  
METHODS MOL. MED. (2000), 42 (VACCINE ADJUVANTS), 121-136.

BROWN  
AEROSOL SCI. TECHNOL. (1996), 24(1), 45-56.

NEWMAN ET AL  
J. PHARM. SCI. (1998), 87(11), 1357-1362.

TODD ET AL  
VACCINE (1997), 15(5), 564-570.

FONTAN ET AL  
INT. J. PHARM. (1991), 73(1), 17-21.

BEREZIN ET AL  
VACCINE (1988), 6(5), 450-456.

LONGENECKER ET AL  
J. PHARM. SCI. (1987), 76(5), 351-355.

M. CEPERLEY  
AU 1641  
MAIL BOX: CM1-7E12  
OFFICE: CM1-8D15  
308-4239

09/647,518

Text

CEPERLEY 09/647,518

=> d bib abs hitstr 1

L7 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
AN 2001:228739 HCAPLUS  
DN 134:271227  
TI Vaccines containing polyoxyethylene sorbitan ester surfactant  
adjuvants  
IN Friede, Martin; Hermand, Philippe; Henerickx,  
Veronique  
PA Smithkline Beecham Biologicals S.A., Belg.  
SO PCT Int. Appl., 25 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001021207	A2	20010329	WO 2000-EP9366	20000922
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
PRAI	GB 1999-22703	A	19990924		
	GB 2000-16685	A	20000706		

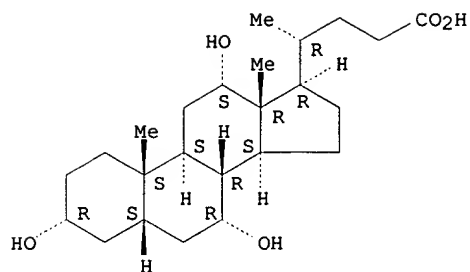
AB The invention relates to a novel adjuvant system comprising a polyoxyethylene sorbitan ester surfactant ~~in combination with an octoxynol~~ and vaccines comprising the adjuvant system together with an antigen. Further provided are methods of manufg. the adjuvants and vaccines and the use of the adjuvants and vaccines in the prophylaxis or therapy of disease. Examples were given for methods used to measure antibody responses in sera and effect of Tween 80 and Triton on the intranasal immunogenicity of inactivated whole influenza virus in mice.

IT 207751-21-1  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; vaccines contg. polyoxyethylene sorbitan ester surfactant adjuvants)  
RN 207751-21-1 HCAPLUS  
CN DNA, d(T-C-G-T-C-G-T-T-T-G-T-C-G-T-T-T-G-T-C-G-T-T) (9CI) (CA INDEX NAME)

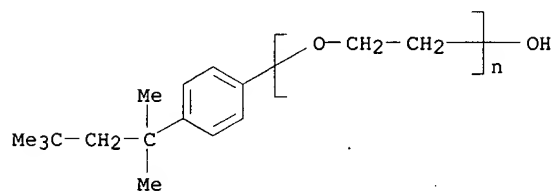
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 81-25-4D, Cholic acid, derivs. 9002-93-1, Triton X-100  
9005-63-4D, Polyoxyethylene sorbitan, esters  
9005-65-6, Tween 80  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(vaccines contg. polyoxyethylene sorbitan ester surfactant adjuvants)  
RN 81-25-4 HCAPLUS  
CN Cholan-24-oic acid, 3,7,12-trihydroxy-, (3.alpha.,5.beta.,7.alpha.,12.alph a.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 9002-93-1 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-  
 .omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9005-63-4 HCAPLUS  
 CN Sorbitan, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9005-65-6 HCAPLUS  
 CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.  
 (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*



=&gt; d bib abs hitstr 2

L7 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:228686 HCAPLUS  
 DN 134:271249  
 TI **Adjuvant** comprising a **polyoxyethylene** alkyl ether or ester and at least one nonionic surfactant  
 IN Friede, Martin; Hermand, Philippe; Henderickx, Veronique  
 PA Smithkline Beecham Biologicals S.A., Belg.  
 SO PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001021152	A1	20010329	WO 2000-EP9368	20000922
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI GB 1999-22700 A 19990924  
 GB 2000-16647 A 20000706

OS MARPAT 134:271249

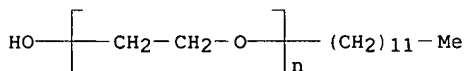
AB The present invention relates to a novel **adjuvant** system comprising a **polyoxyethylene** alkyl ether or ester surfactant in combination with at least 1 addnl. nonionic surfactant. Preferably, the addnl. nonionic surfactant is an **Octoxynol** (the Triton series). The present invention provides the novel **adjuvants**, vaccines comprising them, and methods of their manuf. and their formulation into vaccines. The use of the **adjuvants** or vaccines of the present invention in the prophylaxis or therapy of disease is also provided. The effect of adding Triton X100 to a low and sub-optimal dose of Laureth-9 on the intranasal boosting of tetanus toxoid (TT)-specific serum antibodies was evaluated. Female balb/c mice were primed i.m. with 20% (2x50 pl) of the human dose of the com. DTPa vaccine. Laureth-9 low dose (0.1%) was ineffective in enhancing the boosting response to TT, contrary to the 0.5% dose. However, the adjuvanticity of that formulation was strongly improved by supplementing it with Triton X100. The antibody response elicited was similar to the one induced by the com. DTPa vaccine.

IT 9002-92-0, Polyethylene glycol lauryl ether 9002-93-1, Triton X100 9004-81-3, Polyethylene glycol laurate 9005-00-9, Polyethylene glycol stearyl ether 9005-64-5, Tween 20 9005-65-6, Tween 80 9034-40-6, LRH 9036-19-5, Octoxynol 25322-68-3D, alkyl ethers or esters 199810-71-4

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (adjuvant comprising **polyoxyethylene** alkyl ether or ester and nonionic surfactant)

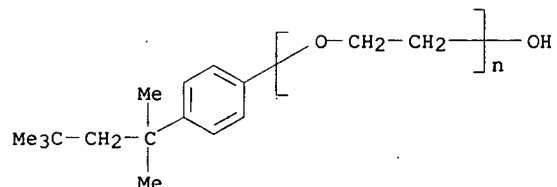
RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

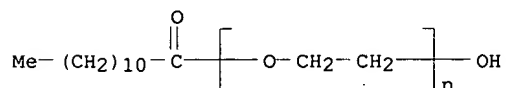


RN 9002-93-1 HCAPLUS

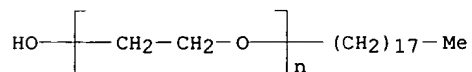
CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9004-81-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxododecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



RN 9005-00-9 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA  
 INDEX NAME)



RN 9005-64-5 HCAPLUS  
 CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA  
 INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

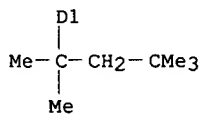
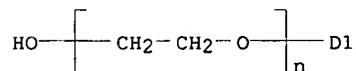
RN 9005-65-6 HCAPLUS  
 CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.  
 (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

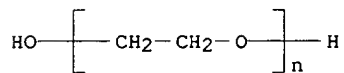
RN 9034-40-6 HCAPLUS  
 CN Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9036-19-5 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[(1,1,3,3-tetramethylbutyl)phenyl]-  
 .omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 25322-68-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 199810-71-4 HCAPLUS  
 CN DNA, d(T-C-C-A-T-G-A-C-G-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RE.CNT 2

RE

- (1) Modi; WO 9636352 A 1996 HCAPLUS
- (2) Smithkline-Beecham; WO 9952549 A 1999 HCAPLUS

=&gt; d bib abs hitstr 3

L7 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:672602 HCAPLUS  
 DN 131:309797  
 TI Adjuvant compositions  
 IN Criede, Martin; Hermand, Philippe  
 PA Smithkline Beecham Biologicals S.A., Belg.  
 SO PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952549	A1	19991021	WO 1999-EP2278	19990329
	W:		AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	AU 9934197	A1	19991101	AU 1999-34197	19990329
	BR 9909915	A	20001226	BR 1999-9915	19990329
	EP 1069910	A1	20010124	EP 1999-915735	19990329
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI		
	NO 2000005051	A	20001121	NO 2000-5051	20001006
PRAI	GB 1998-7805	A	19980409		
	GB 1998-20956	A	19980925		
	WO 1999-EP2278	W	19990329		
OS	MARPAT 131:309797				
AB	The present invention relates to an <b>adjuvant</b> compn. comprising a <b>polyoxyethylene</b> ether or a <b>polyoxyethylene</b> ester, in combination with a pharmaceutically acceptable excipient, and to a vaccine comprising such <b>adjuvant</b> compns. and antigen. In addn., the present invention relates to the use of <b>polyoxyethylene</b> ethers or esters in the manuf. of <b>adjuvant</b> formulations, and vaccine formulations, and their use as medicaments.				
IT	9034-40-6, Luteinizing hormone-releasing hormone 141256-04-4, QS21 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) ( <b>adjuvant</b> compns. comprising <b>polyoxyethylene</b> ether or ester for mucosal vaccine)				
RN	9034-40-6 HCAPLUS				
CN	Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)				

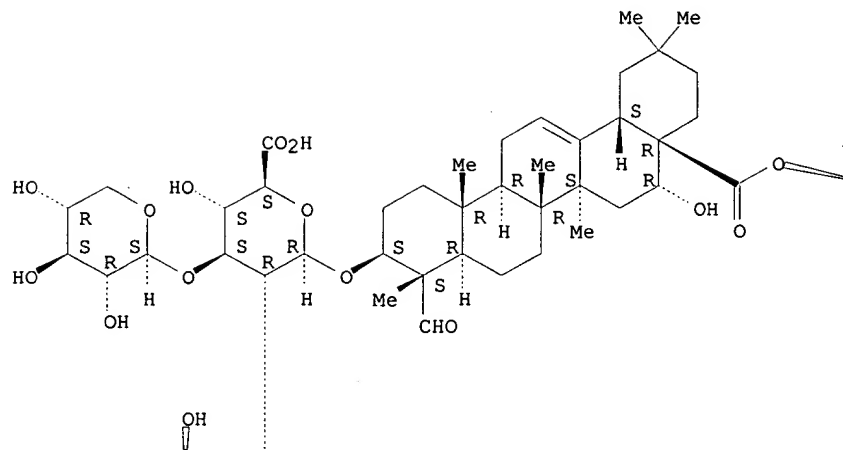
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 141256-04-4 HCAPLUS  
 CN .beta.-D-Glucopyranosiduronic acid, (3.beta.,4.alpha.,16.alpha.)-28-[[O-D-apio-.beta.-D-furanosyl-(1.fwdarw.3)-O-.beta.-D-xylopyranosyl-(1.fwdarw.4)-O-6-deoxy-.alpha.-L-mannopyranosyl-(1.fwdarw.2)-4-O-[5-[5-(.alpha.-L-arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-1-oxooctyl]-6-deoxy-.beta.-D-galactopyranosyl]oxy]-16-hydroxy-23,28-dioxoolean-12-en-3-yl O-.beta.-D-galactopyranosyl-(1.fwdarw.2)-O-[.beta.-D-xylopyranosyl-(1.fwdarw.3)]- (9CI) (CA INDEX NAME)

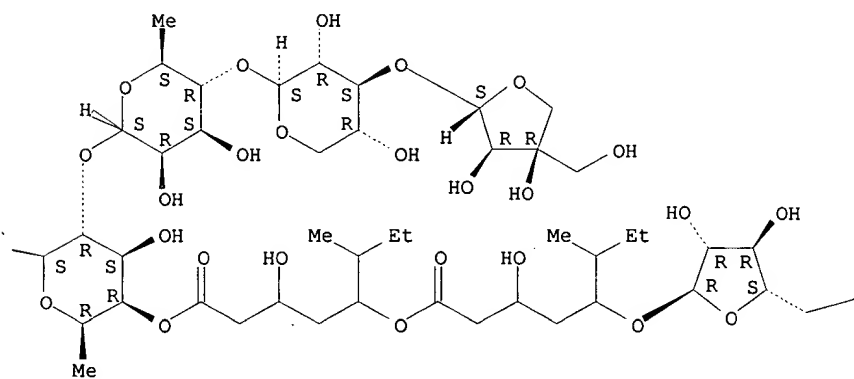
Absolute stereochemistry.

*this applies*

PAGE 1-A



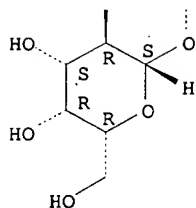
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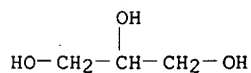
PAGE 1-C

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PAGE 2-A

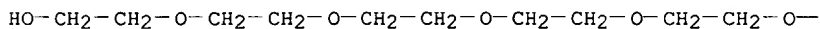


IT 56-81-5D, Glycerol, monoesters 106-08-1  
 3055-99-0 5274-68-0, Polyoxyethylene-4-lauryl  
 ether 7300-85-8 9002-92-0 9012-76-4,  
 Chitosan 13149-87-6 25322-68-3D, esters and ethers  
 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
 26680-10-4, Polylactide 26780-50-7, Polylactide-co-  
 glycolide 190977-41-4 202668-42-6 247116-67-2  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (adjuvant compns. comprising polyoxyethylene ether  
 or ester for mucosal vaccine)  
 RN 56-81-5 HCAPLUS  
 CN 1,2,3-Propanetriol (9CI) (CA INDEX NAME)

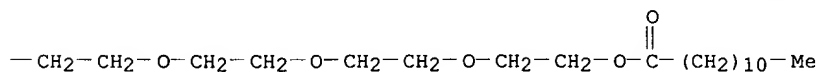


RN 106-08-1 HCAPLUS  
 CN Dodecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaoxahexacos-1-yl ester  
 (9CI) (CA INDEX NAME)

PAGE 1-A

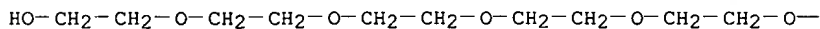


PAGE 1-B

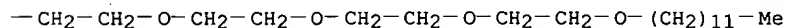


RN 3055-99-0 HCAPLUS  
 CN 3,6,9,12,15,18,21,24,27-Nonaoxanonatriacontan-1-ol (6CI, 7CI, 8CI, 9CI)  
 (CA INDEX NAME)

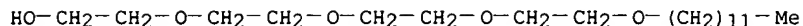
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PAGE 1-B

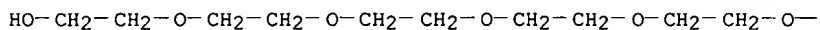


RN 5274-68-0 HCAPLUS  
 CN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

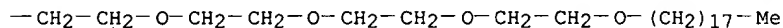


RN 7300-85-8 HCAPLUS  
CN 3,6,9,12,15,18,21,24,27-Nonaoxapentatetracontan-1-ol (9CI) (CA INDEX NAME)

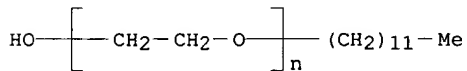
PAGE 1-A



PAGE 1-B



RN 9002-92-0 HCAPLUS  
CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

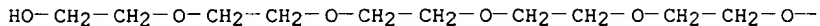


RN 9012-76-4 HCAPLUS  
CN Chitosan (8CI, 9CI) (CA INDEX NAME)

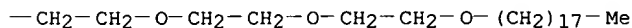
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 13149-87-6 HCAPLUS  
CN 3,6,9,12,15,18,21,24-Octaoxadotetracontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

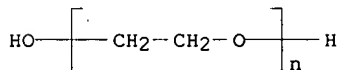
PAGE 1-A



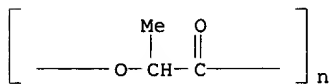
PAGE 1-B



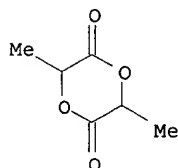
RN 25322-68-3 HCAPLUS  
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)



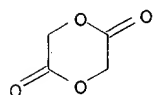
RN 26023-30-3 HCAPLUS  
CN Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] (8CI, 9CI) (CA INDEX NAME)



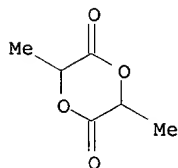
RN 26680-10-4 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, homopolymer (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 95-96-5  
 CMF C6 H8 O4  
 CDES \*



RN 26780-50-7 HCAPLUS  
 CN 1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with 1,4-dioxane-2,5-dione (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 502-97-6  
 CMF C4 H4 O4



CM 2  
 CRN 95-96-5  
 CMF C6 H8 O4  
 CDES \*



RN 190977-41-4 HCAPLUS  
 CN DNA, d(P-thio)(T-C-T-C-C-A-G-C-G-T-G-C-G-C-C-A-T) (9CI) (CA INDEX NAME)  
 \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
 RN 202668-42-6 HCAPLUS  
 CN DNA, d(P-thio)(T-C-C-A-T-G-A-C-G-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME)  
 \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
 RN 247116-67-2 HCAPLUS  
 CN DNA, d(P-thio)(T-C-C-A-T-G-A-G-C-T-T-C-C-T-G-A-C-G-T-T) (9CI) (CA INDEX NAME)  
 \*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
 IT 192778-00-0, GenBank A90868 247214-44-4, PN: WO9952549  
 PAGE: 26 unclaimed DNA



RL: PRP (Properties)  
(unclaimed nucleotide sequence; adjuvant compns.)  
RN 192778-00-0 HCAPLUS  
CN GenBank A90868 (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
RN 247214-44-4 HCAPLUS  
CN PN: WO9952549 PAGE: 26 unclaimed DNA (9CI) (CA INDEX NAME)

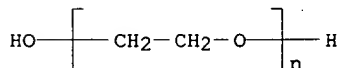
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
RE.CNT 6  
RE  
(1) Carlson, A; US 3919411 A 1975 HCAPLUS  
(2) James, A; WO 9319781 A 1993 HCAPLUS  
(3) Lyfjathroun, H; WO 9417827 A 1994 HCAPLUS  
(4) Macdo, B; WO 9509651 A 1995 HCAPLUS  
(5) Micro Vesicular Systems; WO 8806882 A 1988 HCAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

CEPERLEY 09/647,518

=&gt; d bib abs hitstr

L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:240985 HCAPLUS  
 DN 132:292701  
 TI Novel methods for therapeutic vaccination  
 IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla  
 PA M Amp E Biotech A/s, Den.  
 SO PCT Int. Appl., 220 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020027	A2	20000413	WO 1999-DK525	19991005
	WO 2000020027	A3	20001012		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9958510	A1	20000426	AU 1999-58510	19991005
	EP 1117421	A2	20010725	EP 1999-945967	19991005
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO			
PRAI	DK 1998-1261	A	19981005		
	US 1998-105011	P	19981020		
	WO 1999-DK525	W	19991005		
AB	A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.				
IT	25322-68-3				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adjuvant; weak antigens inserted with foreign T cell epitope as vaccines)				
RN	25322-68-3 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



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L29 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS  
 IC A61K039-00

CC 15-2 (Immunochemistry)  
 Section cross-reference(s): 3, 63

ST weak antigen vaccine cytotoxic T lymphocyte; tumor antigen T cell epitope vaccine

IT Antigens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (17-1A; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (AM-1; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (APC; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (APRIL; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (BAGE; weak antigens inserted with foreign T cell epitope as vaccines)

IT Chemokines  
 (C-X-C, Ena78; weak antigens inserted with foreign T cell epitope as vaccines)

IT CD antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CD33; weak antigens inserted with foreign T cell epitope as vaccines)

IT Glycoproteins, specific or class  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CD40-L (antigen CD40 ligand); weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CD52; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CDC27; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CO17-1A; weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (CS (circumsporozoite), epitope; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (DCC (deleted in colorectal cancer); weak antigens inserted with foreign T cell epitope as vaccines)

IT Antigens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (Dcr3; weak antigens inserted with foreign T cell epitope as vaccines)

IT Proteins, specific or class  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (E6; weak antigens inserted with foreign T cell epitope as vaccines)

IT Transcription factors  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (E7; weak antigens inserted with foreign T cell epitope as vaccines)

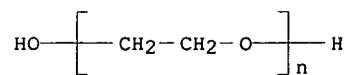
IT Hematopoietin receptors  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (FLT3 receptors; weak antigens inserted with foreign T cell epitope as vaccines)

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=&gt; d bib abs hitstr 1

L30 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:215575 HCAPLUS  
 DN 130:247033  
 TI Synergistic composition and methods for treating neoplastic or cancerous growths and for restoring or boosting hematopoiesis  
 IN Hanna, Nabil; Braslawsky, Gary R.; Hariharan, Kandasamy  
 PA Idec Pharmaceuticals Corporation, USA  
 SO PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9913912	A1	19990325	WO 1998-US18495	19980917
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	ZA 9808461	A	19990330	ZA 1998-8461	19980916
	AU 9895658	A1	19990405	AU 1998-95658	19980917
	EP 1015031	A1	20000705	EP 1998-949313	19980917
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NO 2000001413	A	20000518	NO 2000-1413	20000317
PRAI	US 1997-933359	A	19970918		
	WO 1998-US18495	W	19980917		
AB	A method for treating neoplastic or cancerous growths and for treating cancer patients to restore or boost hematopoiesis comprises administration of a combination of a cytotoxic T-lymphocyte (CTL)-inducing compn. and .gtoreq.1 agent capable of neutralizing or down-regulating the activity of tumor-secreted immunosuppressive factors such as TGF-.beta. and IL-10, sep. or in combination. The CTL inducer is typically a vaccine for enhancing tumor immunity which lacks an immunostimulating peptide component and is formulated as a stable oil-in-water emulsion contg. a micelle-forming agent. The combination produces a synergistic enhancement of the CTL response. Since TGF-.beta. neg. regulates and/or inhibits the growth of hematopoietic cells, the treatment can improve hematopoiesis during cancer therapy. Thus, mice bearing progressively growing ovalbumin-expressing EG7 tumors showed a delay in tumor growth after treatment with 30 .mu.g ovalbumin in Provac adjuvant and 50 .mu.g anti-TGF-.beta. antibodies.				
IT	9005-64-5, Tween 20 9005-65-6, Tween 80 25322-68-3, PEG RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (in vaccine adjuvant; synergistic compn. and methods for treating neoplastic or cancerous growths and for restoring or boosting hematopoiesis)				
RN	9005-64-5 HCAPLUS				
CN	Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)				
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***					
RN	9005-65-6 HCAPLUS				
CN	Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)				
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***					
RN	25322-68-3 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



RE.CNT 3

RE

- (1) Murphy; The Journal of Experimental Medicine 1993, V178, P231 HCAPLUS
- (2) Raychaudhuri; US 5585103 A 1996 HCAPLUS
- (3) Richards; Cell Immunol 1998, V184(2), P85 HCAPLUS

=&gt; d bib abs hitstr 2

L30 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:268384 HCAPLUS

DN 129:3855

TI Adjuvant, in particular as an emulsion, containing a trivalent metal cation and sympathomimetic compound, and vaccine composition containing it

IN Ganne, Vincent; Aucouturier, Jerome

PA Societe D'Exploitation de Produits pour les Industries Chimiques SEPPIC, Fr.

SO PCT Int. Appl., 26 pp.

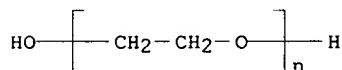
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9817311	A1	19980430	WO 1997-FR1816	19971010
	W: BR, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2754715	A1	19980424	FR 1996-12718	19961018
	FR 2754715	B1	19981113		
	EP 939649	A1	19990908	EP 1997-909390	19971010
	R: BE, DE, ES, FR, GB, IT, NL				
	BR 9712546	A	19991019	BR 1997-12546	19971010
	JP 2000507610	T2	20000620	JP 1998-519016	19971010
PRAI	FR 1996-12718	A	19961018		
	WO 1997-FR1816	W	19971010		
AB	A compn. is disclosed contg.: (i) .gtoreq.1 antigen or .gtoreq.1 in vivo generator of a compd. comprising an amino acid sequence; and (ii) .gtoreq.1 adjuvant. The adjuvant contains a salt of a trivalent metal cation and an org. anion, e.g. aluminum salicylate or aluminum acetate, and .gtoreq.1 sympathomimetic compd. The invention also concerns their use as medicine.				
IT	<u>25322-68-3D. fatty acid esters</u>				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (surfactant; adjuvant emulsion, with trivalent metal cation and sympathomimetic compd., and vaccine compn. contg. it)				
RN	25322-68-3 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



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L30 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

IT **Micelles**

(soln.; adjuvant emulsion, with trivalent metal cation and  
sympathomimetic compd., and vaccine compn. contg. it)

IT 50-70-4D, D-Glucitol, fatty acid esters 56-81-5D, 1,2,3-Propanetriol,  
fatty acid esters 25322-68-3D, fatty acid esters

RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)  
(surfactant; **adjuvant** emulsion, with trivalent metal cation  
and sympathomimetic compd., and vaccine compn. contg. it)

=&gt; d bib abs hitstr 3

L30 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:127592 HCAPLUS

DN 128:261743

TI Elutability of proteins from aluminum-containing vaccine adjuvants by treatment with surfactants

AU Rinella, Joseph V., Jr.; Workman, Ryan F.; Hermodson, Mark A.; White, Joe L.; Hem, Stanley L.

CS Dep. Industrial and Physical Pharmacy, Chemistry, Biochemistry, and Agronomy, Purdue Univ., West Lafayette, IN, 47907, USA

SO J. Colloid Interface Sci. (1998), 197(1), 48-56

CODEN: JCISA5; ISSN: 0021-9797

PB Academic Press

DT Journal

LA English

AB The elutability of proteins from adjuvants in model vaccines composed of ovalbumin adsorbed by aluminum hydroxide adjuvant or lysozyme adsorbed by aluminum phosphate adjuvant following treatment with surfactant solns. was studied. Nonionic (Triton X-100, lauryl maltoside), zwitterionic (lauryl sulfobetaine), anionic (sodium dodecyl sulfate), and cationic (cetylpyridinium chloride, dodecyltrimethylammonium chloride) surfactants were investigated. Cetylpyridinium chloride produced the greatest degree of elution (60%) of ovalbumin from aluminum hydroxide adjuvant. Sodium dodecyl sulfate completely eluted lysozyme from aluminum phosphate adjuvant. The effectiveness of surfactants in removing preadsorbed proteins was directly related to their ability to denature the protein. **Micellar** solubilization and electrostatic repulsion may also contribute to desorption.

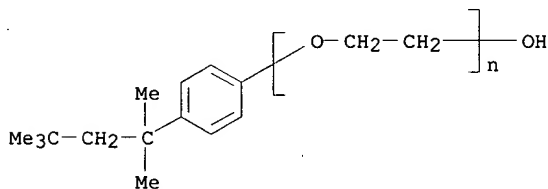
IT 9002-93-1, Triton X-100

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(elutability of proteins from aluminum-contg. vaccine adjuvants by treatment with surfactants)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

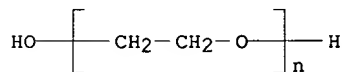




=&gt; d bib abs hitstr 4

L30 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1997:15525 HCAPLUS  
 DN 126:73781  
 TI Multiple antigenic peptide system having adjuvant properties for use in vaccines  
 IN Tam, James P.  
 PA Tam; James P., USA  
 SO U.S., 24 pp. Cont. of U.S. Ser. No. 877,613, abandoned.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	<del>US 5580663</del>	A	19961203	US 1994-331489	19941228
	WO 9322343	A1	19931111	WO 1993-US4179	19930503
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRAI	US 1992-877613		19920501		
	WO 1993-US4179		19930503		
AB	A multiple antigenic peptide system is disclosed that comprises a dendritic core and peptides and a lipophilic anchoring moiety. This peptide system is capable of eliciting an immune response when injected into a mammal; vaccines prep. from the system and methods of use including therapeutic protocols are included. This combination eliminates the need for the inclusion of adjuvants found to be toxic to humans, and facilitates the exponential amplification of the antigenic potential of a vaccine prep. therefrom, as noncovalent amplification by a liposome or micellar form is possible. Further, multiple different antigenic peptides may be attached so that the system may be prep. for administration to concurrently treat diverse ailments, e.g. AIDS and influenza. Thus, 4 copies of a 24-residue peptide (designated B1) of the V3 loop of HIV-1 gp120 were linked to the free N.alpha. and N.epsilon. positions of N.alpha.,N.epsilon.-dilysyl-Lys-Ser-Ser-[N.epsilon.-(tripalmitoyl-S-glycerylcysteinyl)]lysyl-alanine, and the product was incorporated into liposomes which were used to immunize mice. The immunized mice showed a high-titer humoral antibody response, a mitogenic response in spleen cells, a CD4+ T-helper cell response, a cytotoxic T-lymphocyte response, and formation of IL-2 by spleen cells after restimulation.				
IT	25322-68-3D, conjugates with peptides				
	RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(multiple antigenic peptide system having adjuvant properties for use in vaccines)				
RN	25322-68-3 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



Text

CEPERLEY 09/647,518

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L33 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:756545 HCAPLUS  
 DN 1337340220  
 TI Adjuvant comprising a saponin and an immunostimulatory oligonucleotide for manufacture of vaccines  
 IN Friede, Martin; Garcon, Nathalie; Hermand, Philippe  
 PA Smithkline Beecham Biologicals S. A., Belg.  
 SO PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000062800	A2	20001026	WO 2000-EP2920	20000404
	WO 2000062800	A3	20010111		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 1999-8885	A	19990419		
	US 1999-301829	A	19990429		
AB	The present invention relates to adjuvant compns. which are suitable to be used in vaccines. In particular, the adjuvant compns. of the present invention comprises a saponin and an immunostimulatory oligonucleotide, optionally with a carrier. Also provided by the present invention are vaccines comprising the adjuvants of the present invention and an antigen. Further provided are methods of manuf. of the adjuvants and vaccines of the present invention and their use as medicaments. Methods of treating an individual susceptible to or suffering from a disease by the administration of the vaccines of the present invention are also provided.				
IT	9034-40-6, GNRH RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses) (adjuvant comprising a saponin and an immunostimulatory oligonucleotide for manuf. of vaccines)				
RN	9034-40-6 HCAPLUS				
CN	Luteinizing hormone-releasing factor (9CI) (CA INDEX NAME)				

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

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L33 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 IT 11024-24-1, Digitonin 11072-93-8, .beta.-Escin 66594-14-7, Quil A 141256-04-4, QS21 208933-54-4, QS7 218138-45-5, QS17  
 RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (adjuvant comprising a saponin and an immunostimulatory oligonucleotide for manuf. of vaccines)

IT 9002-10-2, Tyrosinase 9034-40-6, GNRH 226408-87-3, Prostate  
 RL: BOC (Biological occurrence); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
 (adjuvant comprising a saponin and an immunostimulatory oligonucleotide for manuf. of vaccines)

=&gt; d bib abs hitstr 2

L33 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:166519 HCAPLUS

DN 130:200945

TI Compositions comprising the adjuvant QS-21 and polysorbate or cyclodextrin as excipient

IN Kensil, Charlotte; Beltz, Gerald A.

PA Aquila Biopharmaceuticals, Inc., USA

SO PCT Int. Appl., 42 pp.

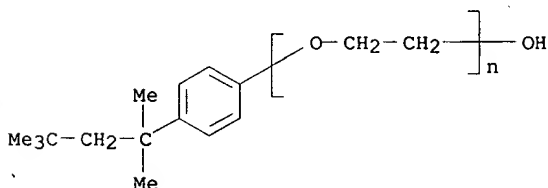
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910008	A1	19990304	WO 1998-US17940	19980828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892107	A1	19990316	AU 1998-92107	19980828
AU 734180	B2	20010607		
EP 1009429	A1	20000621	EP 1998-944600	19980828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1997-57255	P	19970829		
WO 1998-US17940	W	19980828		
AB Certain novel compns. of the adjuvant saponin QS-21 having improved properties are disclosed. The compns. of the present invention are designed (1) to minimize the lytic effects of QS-21, (2) to improve the tolerance of QS-21 contg. formulations in humans or other animals, (3) to stabilize the QS-21 from alk. hydrolysis and/or (4) to maintain the high adjuvant potency of the QS-21 product. These compns. may be employed with vaccines comprising proteins or peptides, polysaccharides, lipids, or nucleic acids. Hydroxypropyl-.beta.-cyclodextrin minimized the lytic effect (increased the hemolytic index) of QS-21 and it hemolytic index was 93 .mu.g/mL at 32 mg/mL.				
IT 9002-93-1, Triton x100 9005-64-5, Polysorbate 20 9005-65-6, Polysorbate 80 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. comprising adjuvant QS-21 and polysorbate or cyclodextrin as excipient)				
RN 9002-93-1	HCAPLUS			
CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9005-65-6 HCAPLUS

CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.  
(9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RE.CNT 9

RE

- (1) Behringwerke Ag; EP 0187286 A 1986 HCAPLUS
  - (2) Dr MaintyKk; JP 06343419 A 1994 HCAPLUS
  - (3) Gerber Jay, D; US 4806350 A 1989 HCAPLUS
  - (4) Peptide Technology Ltd; WO 9104052 A 1991 HCAPLUS
  - (5) Ralph, A; GB 1083815 A 1967 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d kwic 2

L33 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS

ST adjuvant **QS21** polysorbate cyclodextrin excipient

IT 7585-39-9, .beta.-Cyclodextrin 7585-39-9D, .beta.-Cyclodextrin,  
hydroxypropyl ether **9002-93-1**, Triton x100 **9005-64-5**,  
Polysorbate 20 **9005-65-6**, Polysorbate 80 9005-66-7,  
Polysorbate 40 9005-67-8, Polysorbate 60 10016-20-3,  
.alpha.-Cyclodextrin 66594-14-7, Quil a 141256-04-4, **QS-21**  
208933-54-4, **QS-7**

RL: BAC (Biological activity or effector, except adverse); THU  
(**Therapeutic use**); BIOL (Biological study); USES (Uses)  
(comps. comprising **adjuvant QS-21** and polysorbate or  
cyclodextrin as excipient)

=&gt; d bib abs hitstr 3

L33 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:7854 HCAPLUS  
 DN 130:57241  
 TI Oil-in-water vaccine compositions  
 IN Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise  
 PA Smithkline Beecham Biologicals S.A., Belg.  
 SO PCT Int. Appl., 30 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9056414	A1	19981217	WO 1998-EP3479	19980603
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9883365	A1	19981230	AU 1998-83365	19980603
AU 728759	B2	20010118		
EP 999852	A1	20000517	EP 1998-933600	19980603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
BR 9810614	A	20000912	BR 1998-10614	19980603
NO 9906133	A	20000126	NO 1999-6133	19991210
PRAI GB 1997-11990	A	19970611		
WO 1998-EP3479	W	19980603		
AB The present invention relates to improved stable oil-in-water emulsions having an oil droplet diam. of substantially 300-600 nm comprising triglycerides, and their use as vaccine adjuvants.				
IT 9005-65-6, Tween 80				
RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)				
(oil-in-water emulsions as vaccine adjuvants)				
RN 9005-65-6 HCAPLUS				
CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)				

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RE.CNT 4

RE

- (1) Granoff, D; Infection and Immunity 1997, V65(5), P1710 HCAPLUS
- (2) Ott, G; Vaccine 1995, V13(16), P1557 MEDLINE
- (3) Pharmos Corp; WO 9511700 A 1995 HCAPLUS
- (4) Smithkline Beecham Biologicals; WO 9517210 A 1995 HCAPLUS

=&gt; d kwic 3

L33 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 IT 9005-65-6, Tween 80  
 RL: MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (oil-in-water emulsions as vaccine adjuvants)

IT 59-02-9, .alpha.-Tocopherol 111-02-4, Squalene 538-23-8, Tricaprylin 128478-31-9, 3D-MPL 141256-04-4, QS 21  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (oil-in-water emulsions as vaccine adjuvants)

CEPERLEY 09/647,518

CEPERLEY 09/647,518

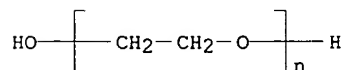
TEXT

CEPERLEY 09/647,518

=&gt; d bib abs hitstr

L36 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:240985 HCAPLUS  
 DN 132:292701  
 TI Novel methods for therapeutic vaccination  
 IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla  
 PA M Amp E Biotech A/s, Den.  
 SO PCT Int. Appl., 220 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020027	A2	20000413	WO 1999-DK525	19991005
	WO 2000020027	A3	20001012		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9958510	A1	20000426	AU 1999-58510	19991005
	EP 1117421	A2	20010725	EP 1999-945967	19991005
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO			
PRAI	DK 1998-1261	A	19981005		
	US 1998-105011	P	19981020		
	WO 1999-DK525	W	19991005		
AB	A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.				
IT	25322-68-3				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adjuvant; weak antigens inserted with foreign T cell epitope as vaccines)				
RN	25322-68-3 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX NAME)				





CEPERLEY 09/647,518

=&gt; d bib abs hitstr 1

L42 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
AN 1998:334648 HCAPLUS  
DN 129:66833  
TI Immune adjuvant comprising synthetic bilayer membrane  
IN Yamada, koji; Okumura, Shiro; Akao, Satoshi  
PA Fukuoka Prefecture, Japan  
SO Jpn. Kokai Tokkyo Koho, 6 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 10139685	A2	<u>19980526</u>	JP 1996-314277	19961111
AB	Synthetic bimol. membrane comprising amphoteric compd. is used for enhancing immune adjuvant in prepn. of antibody. Thus, immune adjuvant comprising ovalbumin and micelle of 12GP2 and 14GP2 were prepd. and used for raising anti-ovalbumin IgG.				
IT	9005-64-5, Tween 20 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (immune adjuvant comprising synthetic bimol. membrane)				
RN	9005-64-5 HCAPLUS				
CN	Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)				

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

=&gt; d bib abs hitstr 2

L42 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS

AN 1988:73342 HCAPLUS

DN 108:73342

TI Synergistic effect of detergents and aluminum phosphate on the humoral immune response to bacterial and viral membrane proteins

AU Teerlink, Tom; Beuvery, E. Coen; Evenberg, Dolf; Van Wezel, Toon L.

CS Dep. Bact. Vaccines, Natl. Inst. Public Health Environ. Hyg. (RIVM), Bilthoven, 3720 BA, Neth.

SO Vaccine (1987), 5(4), 307-14

CODEN: VACCDE; ISSN: 0264-410X

DT Journal

LA English

AB The influence of detergents on the immunogenic activity of the major outer membrane protein of *Neisseria gonorrhoeae* was investigated. Most detergents tested enhanced the immune response. This effect was synergistic with the adjuvant activity of AlPO<sub>4</sub>. The combination of detergent and AlPO<sub>4</sub> showed a stronger adjuvant activity than Freund's complete adjuvant. The adjuvant effect was only obsd. with protein preps. with very low lipopolysaccharide content. The immunostimulating effect of detergents was also obsd. with meningococcal group C polysaccharide conjugated to a *Haemophilus influenzae* type b outer membrane protein and with the fusion protein of measles virus. The influence of some detergent parameters (crit. micelle concn., hydrophile-lipophile balance, and charge) was investigated.

IT 9002-93-1, Triton X-100 9005-64-5, Tween 20

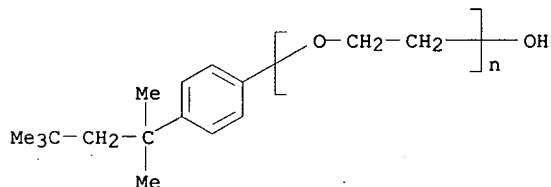
9005-65-6, Tween 80

RL: BIOL (Biological study)

(immune **adjuvant** activity of, aluminum phosphate synergism with, in response to bacterial and viral membrane proteins)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 9005-65-6 HCAPLUS

CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

=&gt; d bib abs hitstr 3

L42 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1986:193210 HCAPLUS  
 DN 104:193210  
 TI Erodible matrix for sustained release bioactive composition  
 IN Snipes, Wallace C.  
 PA Zetachron, Inc., USA  
 SO PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8600802	A1	19860213	WO 1985-US1349	19850717
	W: AU, JP, KP				
	RW: BE, CH, DE, FR, GB, NL				
	CA 1246448	A1	19881213	CA 1985-486711	19850712
	AU 8546388	A1	19860225	AU 1985-46388	19850717
	AU 573149	B2	19880526		
	EP 190255	A1	19860813	EP 1985-903908	19850717
	EP 190255	B1	19921111		
	R: BE, CH, DE, FR, GB, LI, NL				
	JP 61502759	T2	19861127	JP 1985-503436	19850717
PRAI	US 1984-633604		19840723		
	WO 1985-US1349		19850717		

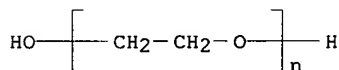
AB A sustained-release oral compn. erodable in **aq. soln.**  
 comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5% of an  
 erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.  
 in the **aq. soln.** Thus, compns. contg. PEGs 1000,  
 4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and  
 indomethacin 25% all released the drug gradually over a period of several  
 h.

IT 25322-68-3

RL: USES (Uses)  
 (molding **adjuvant**, for sustained-release pharmaceuticals with  
 polyethylene glycol matrix)

RN 25322-68-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.omega.-hydroxy- (9CI) (CA INDEX  
 NAME)



=&gt; d kwic 3

L42 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS

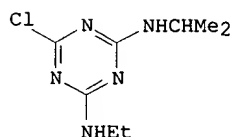
AB A sustained-release oral compn. erodable in **aq. soln.**  
 comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5% of an  
 erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.  
 in the **aq. soln.** Thus, compns. contg. PEGs 1000,  
 4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and  
 indomethacin 25% all. . . .

IT 25322-68-3

RL: USES (Uses)  
 (molding **adjuvant**, for sustained-release pharmaceuticals with  
 polyethylene glycol matrix)

=&gt; d bib abs hitstr 4

L42 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1984:169856 HCAPLUS  
 DN 100:169856  
 TI Surface tension and contact angle of herbicide solutions affected by surfactants  
 AU Singh, Megh; Orsenigo, J. R.; Shah, D. O.  
 CS Inst. Food Agric. Sci., Univ. Florida, Lake Alfred, FL, 33850, USA  
 SO JAOCS, J. Am. Oil Chem. Soc. (1984), 61(3), 596-600  
 CODEN: JJASDH  
 DT Journal  
 LA English  
 GI



AB Contact angle and surface tension were measured for distd. H2O and hard water solns. of **adjuvants** Ortho X-77 [12687-90-0], Span-20 [1338-39-2], Sterox-NJ [59644-67-6], Surfactant-WK [60828-78-6], Triton B-1956, Triton X-114 [9036-19-5], Tween-20 [9005-64-5], and Sun Oil 11E. The same parameters were measured for suspensions of atrazine (I) [1912-24-9] and ametryn [834-12-8] with and without each **adjuvant**. All **adjuvants** reduced surface tension and contact angle of H2O; surfactant-WK was most effective and Tween-20 was least effective. Increasing concn. of surfactants from 0 to 0.1% (vol./vol.) gave progressive redn. in surface tension and contact angle, whereas higher concns., 0.1-2.0% (vol./vol.), had no further effect. Surfactant-WK at 0.1% in H2O reduced surface tension from 72.8 to 27 dynes/cm and contact angle from 110.degree. to 41.degree.. An addnl. increase in Surfactant-WK concn. from 0.1 to 2% did not further reduce surface tension and contact angle. Sun Oil 11E was identical in behavior except that it was less effective than the surfactants. Water hardness .ltoreq.1000 ppm as Ca2+ did not affect surface tension and contact angle in surfactant solns. An **aq. soln.** of I had a higher surface tension and contact angle than ametryn in the absence of surfactants. However, these differences were not obsd. when surfactants were added to either herbicide.

=> d bib abs hitstr 5

L42 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1984:73858 HCAPLUS  
 DN 100:73858  
 TI Effect of pharmaceutical adjuvants on the rectal permeability of drugs.  
 III. Effect of repeated administration and recovery of the permeability  
 AU Nakanishi, Kunio; Masada, Mikio; Nadai, Tanekazu  
 CS Fac. Pharm. Sci., Josai Univ., Sakado, 350-02, Japan  
 SO Chem. Pharm. Bull. (1983), 31(11), 4161-6  
 CODEN: CPBTAL; ISSN: 0009-2363  
 DT Journal  
 LA English  
 AB **Aq. solns.** of Na deoxycholate [302-95-4], Na lauryl sulfate [151-21-3], di-Na ethylenediaminetetraacetate [139-33-3], and polyethylene glycol 400 [25322-68-3] were repeatedly perfused in the rectal lumen of rats. The epithelial cells affected by the **adjuvants** returned to the normal state within 2 h after the pretreatment. However, the goblet cells did not show complete recovery even at 24 h after the pretreatment, and the permeability of the membrane was still higher than the control value at that time. The permeability of the membrane on repeated treatment with the **adjuvants** was not increased as much as on the first treatment.

=&gt; d bib abs hitstr 6

L42 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1977:429028 HCAPLUS  
 DN 87:29028  
 TI Composition with immunostimulant action  
 IN Renoux, Marie Louis; De Montis, Guy; Roche, Alain  
 PA Laboratoires Crinex, Fr.  
 SO Fr. Demande, 9 pp.  
 CODEN: FRXXBL  
 DT Patent  
 LA French  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2306684	A1	19761105	FR 1975-11437	19750411
	FR 2306684	B1	19800208		

AB Immunostimulant compns. comprise propylene glycol [57-55-6], a surfactant, glycerin [56-81-5], and a preservative in a buffered **aq. soln.** For example, an immunostimulant compn. was prepd. comprising propylene glycol 9.83, glycerin 30, Tween 80 [9005-65-6] 6.66, sorbic acid 0.18 vitamin A [11103-57-4] 0.33 g, and pH 5 buffer soln., q.s.p. 100 mL.

IT **9005-65-6**  
 RL: BIOL (Biological study)  
 (in immune **adjuvant** compn.)

RN 9005-65-6 HCAPLUS

CN Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.  
 (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

=&gt; d bib abs hitstr 7

L42 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS

AN 1973:47733 HCAPLUS

DN 78:47733

TI Influence of auxiliary material on pharmaceuticals. 21. Mechanism of interaction between esters of nicotinic acid and poly(oxyethylene) ethers.

AU Ullmann, E.; Thoma, K.; Lippold, B. C.

CS Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger.

SO Arch. Pharm. (Weinheim, Ger.) (1972), 305(11), 797-802

CODEN: ARPMAS

DT Journal

LA German

AB The interactions between surface-active poly(oxyethylene) ethers and esters of nicotinic acid take place in the hydrophobic interior and in the hydrophilic exterior of the **micelles**. The degree of binding of the esters to the **micelles** depends particularly on the physicochem. properties of the esters. The lipophilic hexyl ester, e.g., is bound to a much greater extent than the hydrophilic Et ester. The structure of the surface-active agents has only a small effect. From the exptl. results, conclusions are drawn about the localization of the esters in the **micelles**.

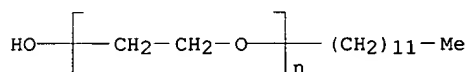
IT 9002-92-0 9005-00-9

RL: BIOL (Biological study)

(pharmaceutical **adjuvants**, nicotinate reaction with)

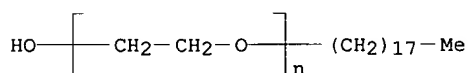
RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9005-00-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 8

L42 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS

AN 1972:429091 HCAPLUS

DN 77:29091

TI Adsorption of drugs from the skeletal muscle of the rats. 3. Effect of water-soluble adjuvants and vehicles on intramuscular absorption

AU Kakemi, Kiichiro; Sezaki, Hitoshi; Okumura, Katsuhiko; Kobayashi, Hiroshi; Furusawa, Shunji

CS Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan

SO Chem. Pharm. Bull. (1972), 20(3), 443-51

CODEN: CPBTAL

DT Journal

LA English

AB The effects of the viscosity and osmotic pressure on the absorption mechanism of isonicotinamide [1453-82-3] and methylisonicotinate [2459-09-8] in the presence of **adjuvants** such as propylene glycol [57-55-6], glycerol [56-81-5], dextran [9004-54-0], polyethylene glycol [25322-68-3], and methyl cellulose [9004-67-5] were studied. From comparison of in vivo i.m. absorption studies in rats with in vitro diffusion expts. it was detd. that the injected soln. was absorbed from the injected site through the muscle fiber space and then the pores of the capillary walls. The latter step may be the rate limiting step in the absorptive process. The absorption mechanism of a drug with water-sol. **adjuvants** did not differ from that in **aqueous soln.** without any **adjuvant**. With small mol. wt. **adjuvants** such as propylene glycol or glycerol there was a correlation between the parenteral absorption rate and the reciprocal of viscosity of an injectable soln.



=&gt; d bib abs hitstr 9

L42 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
AN 1972:94653 HCAPLUS  
DN 76:94653  
TI Biopharmaceutical studies on the effect of adjuvants on the absorption of drugs from drug formulations. 2. Intestinal absorption of sodium p-aminosalicylate from **aqueous solutions** in the presence of surface-active and macromolecular adjuvants  
AU Korossyova, Z.; Zathurecky, L.  
CS Inst. Exp. Pharmacol., Slovak. Acad. Sci., Bratislava, Czech.  
SO Pharmazie (1971), 26(11), 682-5  
CODEN: PHARAT  
DT Journal  
LA German  
AB The surface-active agents Na lauryl sulfate [151-21-3], Septonex [10567-02-9], Tween 80 [9005-65-6], sucrose monolaurate [25339-99-5], sucrose monopalmitate [26446-38-8], and sucrose monostearate [25168-73-4] in concns. below the crit. **micellar** concn., when administered to rats by stomach bound together with Na p-aminosalicylate (I) [133-10-8] (0.01g/100g as 1% soln.), considerably (up to 2-fold) increased the absorption of I. Max. blood levels of I were reached 30 mins after administration both with and without the **adjuvants**. At concns. above the crit. **micellar** concn., these substances had less effect on I absorption. Me cellulose [9004-67-5] and gum arabic slightly increased but also delayed I absorption, due to their high viscosity.

=&gt; d bib abs hitstr 10

L42 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS

AN 1971:480281 HCAPLUS

DN 75:80281

TI Free-flowing, easily wettable particles containing acetylsalicylic acid

IN Boncey, Graham A.; Hedge, Marice J.; Henderson, James Rae

PA Aspro-Nicholas Ltd.

SO Ger. Offen., 25 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2058434	A	19710603	DE 1970-2058434	19701127
	DE 2058434	B2	19800424		
	DE 2058434	C3	19801218		
	GB 1287475	A	19720831	GB 1969-58203	19691128
	ZA 7007915	A	19710825	ZA 1970-7915	19701123
	US 3882228	A	19750506	US 1970-92284	19701123
	IL 35714	A1	19740314	IL 1970-35714	19701124
	IN 129401	A	19750816	IN 1970-129401	19701126
	NL 7017417	A	19710602	NL 1970-17417	19701127
	NL 165928	B	19810115		
	NL 165928	C	19810615		
	FR 2073431	A5	19711001	FR 1970-42668	19701127
	FR 2073431	B1	19740322		
	AT 302533	B	19721025	AT 1970-10713	19701127
	ES 385974	A1	19730501	ES 1970-385974	19701127
	CA 948108	A1	19740528	CA 1970-99296	19701127
	DK 130453	B	19750224	DK 1970-6054	19701127
	SE 383099	B	19760301	SE 1970-16129	19701127
	JP 51006727	B4	19760302	JP 1970-105390	19701128
	US 3887700	A	19750603	US 1973-415247	19731112
PRAI	GB 1969-58203		19691128		
	US 1970-92284		19701123		

AB The title prepn. consists of acetylsalicylic acid particles coated with one or more of the following compds. m. >105.degree.. low mol. wt. amino acids (glycine, methionine), sugars (sucrose, lactose, sugar polymers), sugar alcs. (mannitol, inositol, sorbitol) or mixts. thereof. In addn., the coat contains a wetting agent (cationic, anionic, nonionic types) and (or) a film-forming agent [gums, cellulose derivs., poly(vinylpyrrolidone)]. The ratio of acetylsalicylic acid to the total coating material is preferably between 7.1 to 1.1. Thus, the acetylsalicylic acid is suspended in an **aq. soln.** of the wetting agent. The suspension is treated with a small portion of an **aq. soln.** of the coating material and film-forming agent to form a thin paste. After the remaining soln. of coating material and film-forming agent is added, the suspension obtained is stirred continuously and spray-dried to small particles of which 95% should have a particle size <105 .mu.. Thus coated acetylsalicylic acid particles may be made into water sol. powder or tablets or into effervescent powder or tablets. Six examples are given.

IT 9005-64-5

RL: BIOL (Biological study)  
(pharmaceutical **adjuvant**, in coated powders)

RN 9005-64-5 HCAPLUS

CN Sorbitan, monododecanoate, poly(oxy-1,2-ethanediyl) derivs. (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

=&gt; d bib abs hitstr 1

L48 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:108117 HCAPLUS  
 DN 134:130980  
 TI Preparation of chloride-free organic potassium-enriched compound  
 fertilizer  
 IN Zhang, Xiaochuan  
 PA Peop. Rep. China  
 SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.  
 CODEN: CNXXEV  
 DT Patent  
 LA Chinese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1261065	A	20000726	CN 2000-101170	20000127
AB	<p>The chem. component of the fertilizer comprises N 0-20, P (P2O5) 0-10, K (K2O) 40-25, Zn 0.05-0.01, Fe 0-0.05, Mn 0-0.05, Mo 0-0.05, B 0-0.5, Ti 0-0.005%, and addnl. water and <b>adjuvant</b>. The <b>adjuvant</b> is a <b>aq. soln.</b> contg. surfactant 5-20 part and penetrating agent 5-20 part. The org. acids which form org. salt are selected from citric acid, levulinic acid, hydroxyacetic acid, malic acid, lactic acid, hydroxybutyric acid, maleic acid, oxalic acid, malonic acid, succinic acid, adipic acid, naphthenic acid, lauric acid, etc.; the surfactant from Na lignosulfonate, triacontanol, fatty alc. <b>polyoxyethylene</b> ether, CNF, MF, or WA; and the penetrating agent from JFC or M. The process comprises hydrolyzing furfural or 2-furylcarinol in one or two of org. acid, adding KOH or K2CO3, allowing to react to obtain K salt, adding one or more of borate, carbonate, hydroxide, silicate, phosphate, molybdate and sulfate of Zn, Fe, Cu, Mn, Mg and Ti, adjusting pH to 6-8, adding <b>adjuvant</b>, and mixing. The fertilizer can be absorbed by plant leaf or root, and accelerate plant growth.</p>				

=&gt; d bib abs hitstr 2

L48 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 2001:84475 HCAPLUS

DN 134:183476

TI Oral antibacterial pharmaceutical formulation and method of its preparation

IN Winiarski, Jerzy; Prosciewicz, Boguslaw; Pankowski, Jacek; Korda, Anna; Mroz, Anna; Lewandowska, Maria Bozena; Nowakowska, Krystyna; Wdowiarek, Wlodzimierz; Gwozdz, Ewa; Ryll, Dorota; Kasiak, Irena

PA Polska Akademia Nauk, Instytut Chemii Organicznej, Pol.; Tarchominskie Zaklady Farmaceutyczne POLFA S.A.

SO Pol., 6 pp.

CODEN: POXXA7

DT Patent

LA Polish

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	PL 178281	B1	20000331	PL 1995-307007	19950131

AB The active antibacterial ingredient of the oral formulation is pivaloxymethyl ester of 2,7[2(2-aminothiazolyl-4)-2-methoxyimino]-3'-deacetoxycephalosporinic acid in free form in amts. of 30-70 wt.%. The active ingredient is prepd. from Na salt of 2,7[2(2-aminothiazolyl-4)-2-methoxyimino]-3'-deacetoxycephalosporinic acid in chilled (<5.degree.C) DMF in the presence of triethylamine and pivaloyloxymethyl iodide. After addn. of methanolic soln. of thiourea the reaction mixt. is slowly added to the aq. soln. of NaHCO3 and Na2S2O3 and formed ppt. is recovered, washed, and dried. The formulation is made with 30-70 wt.% of **adjuvant** ingredients (starch, Na starch glycolate, microcryst. cellulose, hydroxypropylcellulose derivs., polyethylene glycol, colloidal silica, Mg stearate, TiO2). The active ingredient is coated with a **polyoxyethylene** surface-active agent (SDS, Tween 80, <5 wt.%) in a solvent that does not dissolve the ester (water). When a homogeneous mixt. with the **adjuvant** ingredients is achieved, appropriate moisture level is adjusted by drying prior to capsule or tablet making. The capsules and tablets made with the surface-active agent showed accelerated rise in blood serum levels of the active ingredient in free acid form as detd. in 12 humans.

=> d bib abs hitstr 3

L48 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:311828 HCAPLUS  
 DN 133:271443  
 TI Aqueous formulation of adjuvant-active nonionic block copolymers  
 AU Todd, Charles W.; Newman, Mark J.  
 CS Vaxcel, Inc., Norcross, GA, USA  
 SO Methods Mol. Med. (2000), 42(Vaccine Adjuvants), 121-136  
 CODEN: MMMEFN  
 PB Humana Press Inc.  
 DT Journal; General Review  
 LA English  
 AB A review, with 22 refs., on **adjuvant**-active nonionic block copolymers that are flexible, linear structures with a core of a hydrophobic polyoxypropylene flanked on both ends by hydrophilic **polyoxyethylene**. Prepn. of copolymer soln. and formulations, dosing and applications, and safety are discussed.  
 RE.CNT 22  
 RE  
 (4) Hem, S; Vaccine Design: The subunit and adjuvant approach 1995, P249 HCAPLUS  
 (6) Hunter, R; J Immunol 1984, V133, P3167 HCAPLUS  
 (9) Kensil, C; Vaccine Design: The subunit and adjuvant approach 1995, P525 HCAPLUS  
 (11) Manetti, R; J Exp Med 1993, V177, P1199 HCAPLUS  
 (12) Newman, M; Critical Rev Therap Drug Carrier Sys 1998, V15, P89 HCAPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d bib abs hitstr 4

L48 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:532142 HCAPLUS

DN 129:265225

TI Design and Development of Adjuvant-Active Nonionic Block Copolymers

AU Newman, Mark J.; Todd, Charles W.; Balusubramanian, Mannersamy

CS Vaxcel Inc., Norcross, GA, 30092, USA

SO J. Pharm. Sci. (1998), 87(11), 1357-1362

CODEN: JPMSAE; ISSN: 0022-3549

PB American Chemical Society

DT Journal

LA English

AB Nonionic block copolymers are surfactants synthesized using propylene oxide and ethylene oxide, and they can be designed so that individual copolymers have unique **vaccine adjuvant** properties. We have designed and produced nonionic block copolymers based on high mol. wt. (MW), 9-15 kDa, cores of polyoxypropylene (POP) coupled with smaller **polyoxyethylene** (POE) end blocks. Copolymers synthesized with <10% POE will spontaneously assemble into 300 nm-3 .mu.m **micelles** or microparticles in **aq. solns.** at physiol. pH, and when formulated with protein, complex microparticles consisting of both the protein and copolymers are formed. The **adjuvant** activity of nonionic block copolymers is influenced by both size and POE content; maximal activity is assocd. with low POE content, 5-10%, and a mol. size of 11-12 kDa. The type of immune response produced is also influenced by the POE content. Copolymers with 10% POE significantly augmented Type 2 helper T-lymphocyte responses, whereas copolymers with lower POE contents augmented both Type 1 and Type 2 helper T-lymphocyte responses. This property allows for **vaccines** to be "customized" by using **adjuvant-active** nonionic block copolymers that will augment the most appropriate types of immune responses.

=&gt; d bib abs hitstr 5

L48 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:359440 HCAPLUS

DN 127:55718

TI Development of an adjuvant-active nonionic block copolymer for use in oil-free subunit vaccine formulations

AU Todd, C. W.; Pozzi, L.-A. M.; Guarnaccia, J. R.; Balasubramanian, M.; Henk, W. G.; Younger, L. E.; Newman, M. J.

CS Vaxcel Inc., Norcross, GA, 30092, USA

SO Vaccine (1997), 15(5), 564-570

CODEN: VACCDE; ISSN: 0264-410X

PB Elsevier

DT Journal

LA English

AB Nonionic block copolymers, synthesized from repeating units of oxypropylene and oxyethylene, can be designed so that individual copolymers have unique phys. properties with differential levels of adjuvant activity. The authors designed high mol. wt. block copolymers that spontaneously assemble into 500 nm-3 .mu.m particles when formulated with protein antigens in aq. solns. at physiol. pH. The adjuvant activity of one of these copolymers, termed CRL 1005, was compared to selected research adjuvants using ovalbumin (OVA) as the prototype vaccine antigen. Suboptimal doses of OVA were formulated with complete and incomplete Freund's adjuvant (CFA/IFA), alum, Quil-A saponins, Ribi Adjuvant System (RAS) or the CRL 1005 copolymer and these formulations were used to immunize C57BL/6 mice. The CRL1005 copolymer appeared to be more potent than either Quil-A or alum and comparable to the RAS formation, based on the nos. of responding mice and the OVA-specific antibody titers. Alum, RAS and Quil-A all augmented the prodn. of IgG1 and IgG2b similarly, whereas only the CFA/IFA boosted IgG2.alpha. levels significantly. The effect of adjuvants on relative antibody affinity was more variable with the CRL 1005 and CFA/IFA inducing antibodies with the highest affinity scores. This high mol. wt. nonionic copolymer is nontoxic in aq. formulations and should therefore be compatible with a wide variety of protein or polysaccharide vaccine antigens.

=> d bib abs hitstr 6

L48 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1994:2671 HCAPLUS  
 DN 120:2671  
 TI Use and mode of action of adjuvants for herbicides: a review of some current work  
 AU Kirkwood, Ralph C.  
 CS Dep. Biosci. Biotechnol., Univ. Strathclyde, Glasgow, G4 0NR, UK  
 SO Pestic. Sci. (1993), 38(2-3), 93-102  
 CODEN: PSSCBG; ISSN: 0031-613X  
 DT Journal; General Review  
 LA English  
 AB A review with 90 refs. The use of surfactants, mineral and vegetable oils, emulsifiers and fertilizer salts, such as ammonium sulfate, can greatly enhance the activity of foliage-applied herbicides. **Adjuvant** herbicide interactions are reviewed with particular ref. to the benefits, including dose redn., enhanced and more consistent herbicide activity, and the nature of underlying mechanisms' the use and role of surfactants receive particular attention. Surfactants are used as activators in com. formulations of many herbicides to improve their foliar absorption and ultimate biol. activity. Current views on their influence are considered in relation to surface phenomena, solubilization of non-polar active ingredients, wax dissoln., cuticle penetration, preferential sites of penetration, membrane permeability and possible systemicity. The importance of a no. of moderating factors (plant, chem. and environmental) is discussed in the light of current work, with particular regard to herbicide polarity, surfactant type, Hydrophile-Lipophile Balance and crit. **micelle** concn. Current studies on the influence of nonionic **polyoxyethylene** surfactants of differing ethylene oxide (EO) content have underlined the importance of EO no. to their activity.



=&gt; d bib abs hitstr 7

L48 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1993:511266 HCAPLUS

DN 119:111266

TI Development of a predictive uptake model to rationalize selection of **polyoxyethylene** surfactant **adjuvants** for foliage-applied agrochemicals

AU Stock, David; Holloway, Peter J.; Grayson, B. Terence; Whitehouse, Paul

CS Dep. Agric. Sci., Univ. Bristol, Bristol, BS18 9AF, UK

SO Pestic. Sci. (1993), 37(3), 233-45

CODEN: PSSCBG; ISSN: 0031-613X

DT Journal

LA English

AB Compn.-concn. relationships between a series of C13/C14 polyoxyethylene primary alc. (AE) surfactants and the foliar uptake enhancement of five model neutral org. compds. were examd. in factorially designed expts. on wheat (*Triticum aestivum* L.) and field bean (*Vicia faba* L.) plants grown under controlled environment conditions. Model compds. were applied to leaves as c.0.2-.mu.L droplets of 0.5 g/L solns. in aq. acetone in the absence or presence of surfactants at 0.2, 1 and 5 g/L. Uptake of the highly water-sol. compd., methylglucose (log octanol-water partition coeff. (P) = -3.0) was best enhanced by surfactants with high E (ethylene oxide) contents (AE15, AE20), whereas those of the lipophilic compds., WL110547 (log P = 3.5) and permethrin (log P = 6.5), were increased more by surfactants of lower E contents, esp. AE6. However, there was little difference between AE6, AE11, AE15 and AE20 in their ability to promote uptake of the two model compds. of intermediate polarity, phenylurea (log P = 0.8) and cyanazine (log P = 2.1). Abs. amts. of compd. uptake were also influenced strongly by both surfactant concn. and plant species. Greatest amts. of uptake enhancement were often obsd. at high surfactant concn. (5 g/L) and on the waxy wheat leaves compared with the less waxy field bean leaves. The latter needed higher surfactant thresholds to produce significant improvements in uptake. Data from the expts. were used to construct a simple response surface model relating uptake enhancement to the E content of the surfactant added and to the physicochem. properties of the compd. to be taken up. Qual. predictions from this model might be useful in rationalizing the design of agrochem. formulations.

=&gt; d kwic 7

L48 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS

TI Development of a predictive uptake model to rationalize selection of **polyoxyethylene** surfactant **adjuvants** for foliage-applied agrochemicals

AB . . . faba L.) plants grown under controlled environment conditions.

Model compds. were applied to leaves as c.0.2-.mu.L droplets of 0.5 g/L

solns. in aq. acetone in the absence or presence of

surfactants at 0.2, 1 and 5 g/L. Uptake of the highly water-sol. compd.,.

=&gt; d bib abs hitstr 9

L48 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1989:227175 HCAPLUS  
 DN 110:227175  
 TI Sustained-release microcapsules containing insecticidal toxins and drugs  
 IN Speaker, Tycho J.; Collett, John H.; Chang, Frank N.; Harvey, William R.;  
 Speaker, Tully J.  
 PA Temple University, USA  
 SO Eur. Pat. Appl., 17 pp.  
 CODEN: EPXXDW  
 DT Patent  
 LA English  
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 299205	A1	19890118	EP 1988-109276	19880610
	EP 299205	B1	19920415		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	US 4797234	A	19890110	US 1987-64859	19870619
	US 4743583	A	19880510	US 1987-75092	19870720
PRAI	US 1987-64820		19870619		
	US 1987-64821		19870619		
	US 1987-64859		19870619		
	US 1987-75092		19870720		

AB Sustained-release microcapsules comprise a permeable anisotropic salt film encapsulating a proteinaceous biol. active core. The film is the reaction product of a Lewis base or salt thereof, in a slightly polar org. solvent, with a polyfunctional partially hydrophilic, partially lipophilic Lewis acid or salt thereof in aq. soln. or suspension. Adjuvants may be optionally present. The slightly polar org. solvent is a nondenaturing solvent or solvent complex capable of solubilizing or suspending the proteinaceous material. An aq. soln. (10 mL) contg. 1 g arabic acid was stirred with a soln. of anhyd. piperazine (amt. stoichiometrically equiv. with arabic acid) and 0.005 g somatotrophic hormone in butyrolactone (10 mL soln.), to give, after centrifuging, microcapsules.

=&gt; d kwic 9

L48 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AB . . . thereof, in a slightly polar org. solvent, with a polyfunctional partially hydrophilic, partially lipophilic Lewis acid or salt thereof in aq. soln. or suspension. Adjuvants may be optionally present. The slightly polar org. solvent is a nondenaturing solvent or solvent complex capable of solubilizing or suspending the proteinaceous material. An aq. soln. (10 mL) contg. 1 g arabic acid was stirred with a soln. of anhyd. piperazine (amt. stoichiometrically equiv. with arabic acid).  
 IT 107-15-3, Ethylenediamine, biological studies 9003-01-4D, crosslinked with polyalkenyl ethers 9003-11-6, Polyoxyethylene-polyoxypropylene 106392-12-5, Polyoxyethylene-polyoxypropylene block copolymer  
 RL: BIOL (Biological study)  
 (as microencapsulation adjuvant, for insecticidal toxins and drugs)

=> d bib abs hitstr 10

L48 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
AN 1986:83712 HCAPLUS  
DN 104:83712  
TI The effect of adjuvants and oil carriers on photodecomposition of 2,4-D, bentazon, and haloxyfop  
AU Harrison, S. Kent; Wax, Loyd M.  
CS Dep. Agron., Univ. Illinois, Urbana, IL, 61801, USA  
SO Weed Sci. (1986), 34(1), 81-7  
CODEN: WEESA6; ISSN: 0043-1745  
DT Journal  
LA English  
AB Lab. photolysis rates of 2,4-D [94-75-7], bentazon [25057-89-0], and haloxyfop [69806-34-4] in dil. aq. soln. were enhanced by **adjuvants**. Addn. (vol./vol.) of 1.0% petroleum oil conc., 1.0% soybean oil conc., and 0.15% emulsifier package enhanced herbicide photolysis rates more than addn. of 0.15% oxysorbic [9005-64-5] (20 POE) (**polyoxyethylene** sorbitan monolaurate). Bioassays showed that phytotoxicity of photolyzed herbicide solns. was neg. correlated with time of exposure to UV light. Addn. of 0.85% acetophenone [98-86-2] to aq. herbicide solns. contg. 0.15% oxysorbic strongly sensitized photodegrdn. of 2,4-D, and to a lesser extent, haloxyfop. Acetophenone had no effect on bentazon photolysis in the presence of oxysorbic. In another study, herbicides were dissolved in white mineral oil or once-refined soybean oil and exposed to UV light. After a 6-h exposure, there was 92% loss of haloxyfop in mineral oil and 36% loss in soybean oil. There was no difference between oils in affecting the photolysis rate of 2,4-D or bentazon.

=> d bib abs hitstr 11

L48 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1969:94799 HCAPLUS  
 DN 70:94799  
 TI Effects of Tween 80 and Freon 113 on measles virus  
 AU Parisius, Wolf; Macmorine, Hilda G.  
 CS Connaught Med. Res. Lab., Univ. Toronto, Willowdale, Ont., Can.  
 SO Appl. Microbiol. (1969), 17(3), 379-83  
 CODEN: APMBAY  
 DT Journal  
 LA English  
 AB Measles vaccines were prepd. from the same virus fluids by inactivation with HCHO or by extn. with ether, ethyl acetate, or Freon 113 in the presence of Tween 80. Tests of antigenic potency, based on antibody levels in guinea pigs, showed that the HCHO-inactivated vaccines were more potent than the solvent-inactivated preps. and had the addnl. advantage of long shelf life. Residual Tween 80 in the solvent-extd. vaccines resulted in marked loss of immunogenic potency without significant loss of hemagglutinating activity. Neither extn. with organic solvents nor exhaustive dialysis efficiently removed Tween 80 from aq. solns.

=> d kwic 11

L48 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AB . . . potency without significant loss of hemagglutinating activity. Neither extn. with organic solvents nor exhaustive dialysis efficiently removed Tween 80 from aq. solns.  
 IT Sorbitan, monooleate, polyoxyethylene derivs.  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
 (measles virus response to, vaccine antigenicity in relation to)

=&gt; d bib abs hitstr 12

L48 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1968:446063 HCAPLUS

DN 69:46063

TI Inactivation of myxoviruses

IN Kanarek, Alexander D.

PA Wellcome Foundation Ltd.

SO Ger., 7 pp.

CODEN: GWXXAW

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 1270223		19680612		
PRAI	GB		19640320		

AB Aq. suspensions of myxoviruses, (I), were inactivated with concurrent preservation of antigenicity by treating with 8-30 vol. % of chlorinated or chlorinated and fluorinated hydrocarbons, at pH 6-8 in the presence of .gtoreq.0.05 wt. % of a nonionic wetting agent. Thus, a 6.25% by vol. **aq. soln. of polyoxyethylene** sorbitan monooleate (9 ml.) was added to the centrifuged culture liquor (441 ml.) of a measles virus grown on a chick embryo tissue culture and then intimately mixed with Cl2C:CCl2 (50 ml.) at room temp. for 1 hr. The solvent was centrifuged and the aq. phase retained as a primary **vaccine**. Also inactivated were influenza (A, B and C), Newcastle disease, rubella, parainfluenza and respiratory syncytial viruses with other hydrocarbons, e.g., CCl4, ClCH:CCl2, Cl2CFCF2Cl3, (Cl3C)2CH2 and Cl2C:CClCCl:CCl2, in the presence of, e.g., **polyoxyethylene** ethers of partial esters of lauric, palmitic or stearic acids. cf. U.S. 2,798,835 (CA 51: 15072i).

=&gt; d kwic 12

L48 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AB . . . at pH 6-8 in the presence of .gtoreq.0.05 wt. % of a nonionic wetting agent. Thus, a 6.25% by vol. **aq. soln. of polyoxyethylene** sorbitan monooleate (9 ml.) was added to the centrifuged culture liquor (441 ml.) of a measles virus grown on a . . . (50 ml.) at room temp. for 1 hr. The solvent was centrifuged and the aq. phase retained as a primary **vaccine**. Also inactivated were influenza (A, B and C), Newcastle disease, rubella, parainfluenza and respiratory syncytial viruses with other hydrocarbons, e.g., CCl4, ClCH:CCl2, Cl2CFCF2Cl3, (Cl3C)2CH2 and Cl2C:CClCCl:CCl2, in the presence of, e.g., **polyoxyethylene** ethers of partial esters of lauric, palmitic or stearic acids. cf. U.S. 2,798,835 (CA 51: 15072i).

=&gt; d bib abs hitstr 13

L48 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1960:70822 HCAPLUS  
 DN 54:70822  
 OREF 54:13564a-d  
 TI Mouthwashes  
 IN Bouchal, Alexander W.  
 PA Colgate-Palmolive Co.  
 DT Patent  
 LA Unavailable  
 FAN.CNT 1

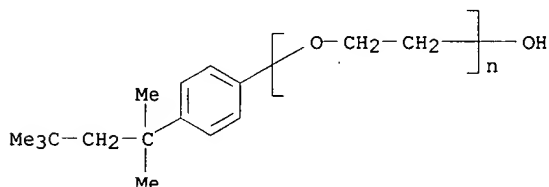
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2921885		19600119	US	
AB	<p>A soln. of 0.3% (diisobutylcresoxyethoxyethyl)dimethylbenzylammonium chloride (I) and 0.2% Na N-lauroylsarcosine (II) is prepd. in distd. H2O. For example, standard disk-halo tests of this soln. against Micrococcus pyogenes, var. aureus (Staphylococcus aureus) showed that this compn. prevented bacterial growth over an area 135% greater than that in which 0.03% of I alone was used. Doubling the amt. of I to 0.06% resulted in only a 15% increase in area of bacteriostasis over that of the 3% soln. Similarly, an aq. soln. contg. 0.03% I, 0.2% II, and 0.5% HO(C2H4O)a(C3H7O)b(C2H4O)cH (IV) in which the polypropylene oxide has a mol. wt. of 1500-800 and the polymerized ethylene oxide comprises 80-90% by wt. showed that this soln. prevented growth in an area 153% greater than that obtained with I alone. When 0.25% polyoxyethylene tridecyl alc. having about 12 ethylene oxide groups replaces the 0.5% IV in the above formula, the area of no bacterial growth is 300% more than that from the use of I alone. A soln. of I, 0.2% Na N-lauroyl-.beta.-alanine, and 0.5% IV in distd. H2O prevented bacterial growth in an area 52% greater than that obtained with I alone. A mouth rinse (a) was prepd. contg. I 0.03, II 0.2, IV 0.5, EtOH 15, adjuvants 0.2, and H2O 84.07%. Standard disk-halo tests against S. aureus and Lactobacillus K. gave a halo diam. of 23.5 mm. and 21.2 mm., resp. A mouth rinse (b) contained I 0.03, II 0.2, IV 0.5, EtOH 5, glycerol 0.1, adjuvants 0.1, and H2O 84.17%. A halo of 22.5 mm. was obtained against S. aureus and Lactobacillus. The mouth rinse (a) was tested in vivo by a panel of 12 persons and found to be more effective as compared with other mouth rinses.</p>				

CEPERLEY 09/647,518

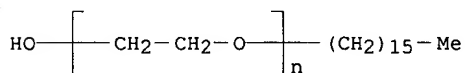
=&gt; d bib abs hitstr 1

L36 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1988:73342 HCAPLUS  
 DN 108:73342  
 TI Synergistic effect of detergents and aluminum phosphate on the humoral immune response to bacterial and viral membrane proteins  
 AU Teerlink, Tom; Beuvery, E. Coen; Evenberg, Dolf; Van Wezel, Toon L.  
 CS Dep. Bact. Vaccines, Natl. Inst. Public Health Environ. Hyg. (RIVM), Bilthoven, 3720 BA, Neth.  
 SO Vaccine (1987), 5(4), 307-14  
 CODEN: VACCDE; ISSN: 0264-410X  
 DT Journal  
 LA English  
 AB The influence of detergents on the immunogenic activity of the major outer membrane protein of *Neisseria gonorrhoeae* was investigated. Most detergents tested enhanced the immune response. This effect was synergistic with the **adjuvant** activity of AlPO<sub>4</sub>. The combination of detergent and AlPO<sub>4</sub> showed a stronger **adjuvant** activity than Freund's complete **adjuvant**. The **adjuvant** effect was only obsd. with protein prepns. with very low lipopolysaccharide content. The **immunostimulating** effect of detergents was also obsd. with meningococcal group C polysaccharide conjugated to a *Haemophilus influenzae* type b outer membrane protein and with the fusion protein of measles virus. The influence of some detergent parameters (crit. micelle concn., hydrophile-lipophile balance, and charge) was investigated.  
 IT 9002-93-1, Triton X-100 9004-95-9, Brij 58  
 9004-99-3, Myrj 45  
 RL: BIOL (Biological study)  
 (immune **adjuvant** activity of, aluminum phosphate synergism with, in response to bacterial and viral membrane proteins)  
 RN 9002-93-1 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

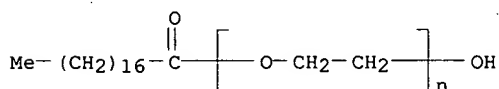
see above



RN 9004-95-9 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9004-99-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)



CEPERLEY 09/647,518



=&gt; d bib abs hitstr 2

L36 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS

AN 1986:532044 HCAPLUS

DN 105:132044

TI Immunogenic complex and its use as an immune stimulant, vaccines and reagent

IN Morein, Bror

PA Swed.

SO Eur. Pat. Appl., 65 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 180564	A2	19860507	EP 1985-850326	19851016
	EP 180564	A3	19880601		
	EP 180564	B1	19910717		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 65186	E	19910815	AT 1985-850326	19851016
	CA 1275042	A1	19901009	CA 1985-493583	19851022
	FI 8504158	A	19860502	FI 1985-4158	19851023
	FI 86801	B	19920715		
	FI 86801	C	19921026		
	ZA 8508157	A	19860625	ZA 1985-8157	19851023
	DK 8504985	A	19860502	DK 1985-4985	19851030
	DK 166653	B1	19930628		
	NO 8504355	A	19860502	NO 1985-4355	19851031
	NO 167076	B	19910624		
	NO 167076	C	19911002		
	JP 61129136	A2	19860617	JP 1985-245270	19851031
	JP 07116056	B4	19951213		
	ES 548412	A1	19861201	ES 1985-548412	19851031
	AU 8549383	A1	19860508	AU 1985-49383	19851106
	AU 589915	B2	19891026		
	ZA 8607792	A	19870527	ZA 1986-7792	19861014
	CA 1275246	A1	19901016	CA 1986-520464	19861015
	WO 8702250	A1	19870423	WO 1986-SE480	19861016
	W: AU, DK, FI, JP, NO, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8664752	A1	19870505	AU 1986-64752	19861016
	AU 590904	B2	19891123		
	EP 242380	A1	19871028	EP 1986-906026	19861016
	EP 242380	B1	19910403		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	JP 63501078	T2	19880421	JP 1986-505483	19861016
	JP 07051514	B4	19950605		
	ES 2002532	A6	19880816	ES 1986-2624	19861016
	AT 62135	E	19910415	AT 1986-906026	19861016
	US 5254339	A	19931019	US 1987-70920	19870601
	FI 8702647	A	19870615	FI 1987-2647	19870615
	FI 86597	B	19920615		
	FI 86597	C	19920925		
	NO 8702484	A	19870615	NO 1987-2484	19870615
	NO 168806	B	19911230		
	NO 168806	C	19920408		
	DK 8703029	A	19870814	DK 1987-3029	19870615
	DK 165360	B	19921116		
	DK 165360	C	19930405		
PRAI	SE 1984-5493		19841101		
	EP 1985-850326		19851016		
	EP 1986-906026		19861016		
	WO 1986-SE480		19861016		
	WO 1987-SE480		19870601		

AB An immunogenic complex is prepd. by (1) mixing antigenic biol. material with a solubilizing agent to form a complex between the solubilizing agent and proteins or peptides in the material; (2) transferring the proteins or peptides from the complex with solubilizing

agent to a soln. of a glycoside with which they formed a complex serving as a carrier mol.; (3) coupling .gtoreq. 1 **antigens** or haptens to the carrier. For example, envelope proteins from influenza virus strain PR8 were solubilized with 20% N-decanoyl-N-methylglucamine and sepd. from the core structure by centrifugation through 20% sucrose contg. the detergent at a concn. > than the crit. **micellar** concn. The collected proteins, with 0.1% Quil A (saponin) added to form a complex, were dialyzed against 0.9% NaCl and coupled to LH-RH with glutaraldehyde. Mice immunized with this LH-RH conjugate showed a strong immune response with no side effects.

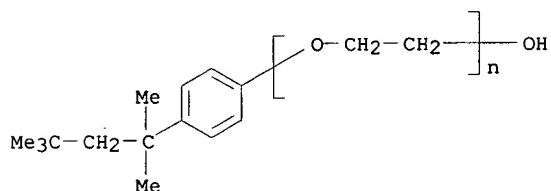
IT 9002-93-1

RL: BIOL (Biological study)

(as solubilizer, in **antigen** carrier prepn.)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 3

L36 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2001 ACS

AN 1985:600769 HCAPLUS

DN 103:200769

TI Contribution to the investigation of **micellar** solubilization - specific case of surfactant mixtures

AU Vaution, Catherine; Treiner, Claude

CS Fac. Pharm., Univ. Paris-Sud, Chatenay-Malabry, 92290, Fr.

SO S.T.P. Pharma (1985), (4), 333-40

CODEN: STPPEF

DT Journal

LA French

AB **Micellar** solubilization is generally characterized by soly. coeff. or partition coeff. The soly. coeff (k) is given by  $C_t / C_{aq} = 1 + kC_s$ ; where  $C_t$  = total concn. of the solute present in the **micellar** soln.,  $C_{aq}$  = concn. of the solute dissolved in water, and  $C_s$  = concn. of **adjuvant** (in the case of **micellar** solubilization, the **adjuvant** is a surfactant). The value of partition coeff. K (also described by various math. equations) is characteristic of the surfactant used for a given temp. and pressure. The value is const. under conditions in which the solute behaves as an ideal compd. in the 2 phases (a **micellar** soln. consists of an aq. phase and inseparable **micellar** phase or pseudo-phase). During **micellar** solubilization, the solute is always weakly sol. in the aq. phase. This implies that the solute-solute interaction can be considered as 0 and the activity coeff. (f) = 1. On the contrary, the solute is bound in the **micelles** at relatively elevated concns. In this case relatively strong interactions can occur in the **micellar** phase. The pseudo-phase model was validated by detg. the logarithm of partition coeff. in a **micellar** system as a function of logarithm of partition coeff. in a biphasic system. Trimethyldodecylammonium bromide [1119-94-4] (cationic surfactant) and Na dodecyl sulfate [151-21-3] (anionic surfactant) were used as the model compds. **Micellar** solubilization was also demonstrated in mixed **micelle** systems. The solubilizing capacity and the partition coeff. were detd. as a function of effective compn. of mixed **micelles**.

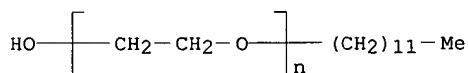
IT 9002-92-0

RL: PROC (Process)

(micellar solubilization of)

RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



CEPERLEY 09/647,518

=&gt; d bib abs hitstr 1

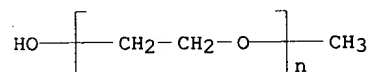
L39 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1998:629681 HCAPLUS  
 DN 130:57111  
 TI Synthesis, physicochemical properties and immunoadjuvant activity of water-soluble phosphazene polyacids  
 AU Andrianov, Alexander K.; Sargent, Jonathan R.; Sule, Sameer S.; Le Golvan, Mark P.; Woods, Angela L.; Jenkins, Sharon A.; Payne, Lendon G.  
 CS Virus Research Institute, Inc., Cambridge, MA, 02138, USA  
 SO J. Bioact. Compat. Polym. (1998), 13(4), 243-256  
 CODEN: JBCPEV; ISSN: 0883-9115  
 PB Technomic Publishing Co., Inc.  
 DT Journal  
 LA English  
 AB Mixed-substituted polyphosphazenes contg. carboxylic acid and alkyl ether side groups were synthesized and characterized. Physicochem. properties of phosphazene polyacids in aq. solns. were investigated as a function of copolymer structure and compn. The immunoadjuvant activity of polyphosphazenes was evaluated by studying the effect of copolymers on the immunogenicity of the influenza virus in mice. The polyphosphazenes demonstrated the ability to enhance the immune response as compared to the levels elicited by the vaccine alone.  
 IT 109-86-4DP, 2-Methoxyethanol, reaction products with polyphosphazene, hydrolyzed 111-77-3DP, 2-(2-Methoxyethoxy)ethanol, reaction products with polyphosphazene, hydrolyzed 9004-74-4DP, Polyethylene glycol methyl ether, reaction products with polyphosphazene, hydrolyzed  
 RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. and physicochem. properties and immunoadjuvant activity of water-sol. phosphazene polyacids)  
 RN 109-86-4 HCAPLUS  
 CN Ethanol, 2-methoxy- (8CI, 9CI) (CA INDEX NAME)

HO-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>

RN 111-77-3 HCAPLUS  
 CN Ethanol, 2-(2-methoxyethoxy)- (6CI, 8CI, 9CI) (CA INDEX NAME)

MeO-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-OH

RN 9004-74-4 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 13

RE

- (1) Allcock, H; Biodegradable Polymers as Drug Delivery Systems 1990, P163 HCAPLUS
  - (2) Allcock, H; Biomaterials 1996, V17, P2295 HCAPLUS
  - (3) Allcock, H; Macromolecules 1986, V19, P1508 HCAPLUS
  - (4) Allcock, H; Macromolecules 1989, V22, P75 HCAPLUS
  - (5) Allcock, H; Macromolecules 1996, V29, P1313 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d bib abs hitstr 2

L39 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:127592 HCAPLUS

DN 128:261743

TI Elutability of proteins from aluminum-containing **vaccine adjuvants** by treatment with surfactants

AU Rinella, Joseph V., Jr.; Workman, Ryan F.; Hermodson, Mark A.; White, Joe L.; Hem, Stanley L.

CS Dep. Industrial and Physical Pharmacy, Chemistry, Biochemistry, and Agronomy, Purdue Univ., West Lafayette, IN, 47907, USA

SO J. Colloid Interface Sci. (1998), 197(1), 48-56

CODEN: JCISA5; ISSN: 0021-9797

PB Academic Press

DT Journal

LA English

AB The elutability of proteins from **adjuvants** in model **vaccines** composed of ovalbumin adsorbed by aluminum hydroxide **adjuvant** or lysozyme adsorbed by aluminum phosphate **adjuvant** following treatment with surfactant solns. was studied. Nonionic (Triton X-100, lauryl maltoside), zwitterionic (lauryl sulfobetaine), anionic (sodium dodecyl sulfate), and cationic (cetylpyridinium chloride, dodecyltrimethylammonium chloride) surfactants were investigated. Cetylpyridinium chloride produced the greatest degree of elution (60%) of ovalbumin from aluminum hydroxide **adjuvant**. Sodium dodecyl sulfate completely eluted lysozyme from aluminum phosphate **adjuvant**. The effectiveness of surfactants in removing preadsorbed proteins was directly related to their ability to denature the protein. **Micellar** solubilization and electrostatic repulsion may also contribute to desorption.

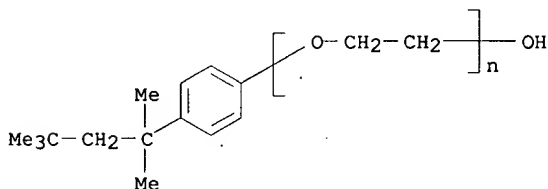
IT 9002-93-1, Triton X-100

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(elutability of proteins from aluminum-contg. **vaccine adjuvants** by treatment with surfactants)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



$$\text{Me}_3\text{C}-\text{CH}_2-\underset{\text{Me}}{\overset{\text{Me}}{\text{C}}}-\text{C}_6\text{H}_4-\left[\text{O}-\text{CH}_2-\text{CH}_2\right]_n-\text{OH}$$

CEPERLEY 09/647,518

=&gt; d bib abs hitstr 1

L40 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1998:208885 HCAPLUS  
 DN 128:190536  
 TI Enhancement of the Diffusion of Active Ingredients in Barley Leaf  
 Cuticular Wax by Monodisperse Alcohol Ethoxylates  
 AU Burghardt, Markus; Schreiber, Lukas; Riederer, Markus  
 CS Lehrstuhl fuer Botanik II Oekophysiologie und Vegetationsoekologie  
 Biozentrum, Universitaet Wuerzburg, Wuerzburg, D-97082, Germany  
 SO J. Agric. Food Chem. (1998), 46(4), 1593-1602  
 CODEN: JAFCAU; ISSN: 0021-8561  
 PB American Chemical Society  
 DT Journal  
 LA English  
 AB Rates of uptake of active ingredients (ai) across the plant cuticle are  
 enhanced by the action of alc. ethoxylate (AE) **adjuvants**. The  
 partitioning of monodisperse AE between **aq. solns.** and  
 isolated cuticular wax from barley (*Hordeum vulgare* L.) leaves was  
 investigated. Quant. structure-property relationships for wax/water  
 partition coeffs. (K<sub>wax/w</sub>) and max. AE concns. in the wax (c<sub>waxmax</sub>) were  
 established. In the presence of AE, the diffusion coeffs. of six ai in  
 cuticular wax increased by factors of up to 125. AE effects were linearly  
 related to their resp. c<sub>waxmax</sub>, suggesting a common intrinsic activity.  
 AE had higher effects on the diffusion coeffs. of large ai than on those  
 of smaller ones. Conclusions are drawn concerning the mechanism of AE  
 action on the phys. structure of cuticular waxes.  
 IT 112-34-5, Diethylene glycol monobutyl ether 3055-93-4,  
 Diethylene glycol monododecyl ether 3055-94-5, Triethylene  
 glycol monododecyl ether 3055-95-6, Pentaethylene glycol  
 monododecyl ether 3055-96-7, Hexaethylene glycol monododecyl  
 ether 3055-97-8, Heptaethylene glycol monododecyl ether  
 3055-98-9, Octaethylene glycol monododecyl ether 5274-68-0  
 , Tetraethylene glycol monododecyl ether 5698-39-5, Octaethylene  
 glycol monohexadecyl ether 19327-39-0, Tetraethylene glycol  
 monooctyl ether 23244-49-7, Pentaethylene glycol monodecyl ether  
 24233-81-6, Octaethylene glycol monodecyl ether 25961-89-1  
 , Triethylene glycol monohexyl ether 27847-86-5, Octaethylene  
 glycol monotetradecyl ether 40036-79-1, Heptaethylene glycol  
 monotetradecyl ether  
 RL: AGR (Agricultural use); BAC (Biological activity or effector, except  
 adverse); PRP (Properties); BIOL (Biological study); USES (Uses)  
 (enhancement of the diffusion of active ingredients in barley leaf  
 cuticular wax by monodisperse alc. ethoxylates)  
 RN 112-34-5 HCAPLUS  
 CN Ethanol, 2-(2-butoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)

$$\text{n-BuO}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{OH}$$

RN 3055-93-4 HCAPLUS  
 CN Ethanol, 2-[2-(dodecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

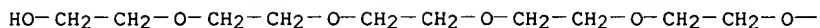
$$\text{HO}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-(\text{CH}_2)_{11}-\text{Me}$$

RN 3055-94-5 HCAPLUS  
 CN Ethanol, 2-[2-[2-(dodecyloxy)ethoxy]ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA  
 INDEX NAME)

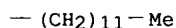
$$\text{HO}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-(\text{CH}_2)_{11}-\text{Me}$$

RN 3055-95-6 HCAPLUS  
 CN 3,6,9,12,15-Pentaoxaheptacosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

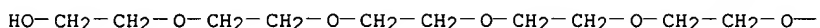


PAGE 1-B

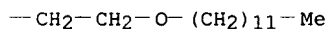


RN 3055-96-7 HCAPLUS  
CN 3,6,9,12,15,18-Hexaoxatriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

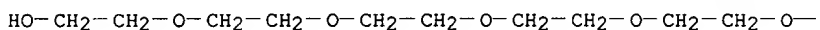


PAGE 1-B

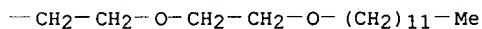


RN 3055-97-8 HCAPLUS  
CN 3,6,9,12,15,18,21-Heptaoxatritriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

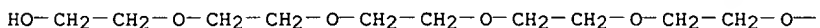


PAGE 1-B

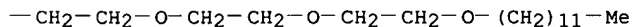


RN 3055-98-9 HCAPLUS  
CN 3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

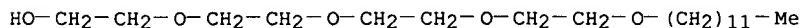
PAGE 1-A



PAGE 1-B



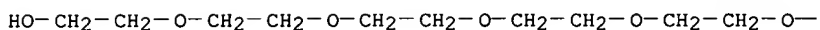
RN 5274-68-0 HCAPLUS  
CN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



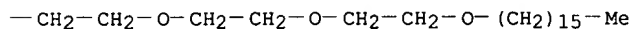
RN 5698-39-5 HCAPLUS  
CN 3,6,9,12,15,18,21,24-Octaoxatetracontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)



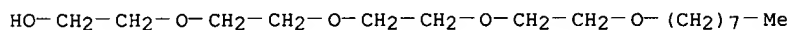
PAGE 1-A



PAGE 1-B

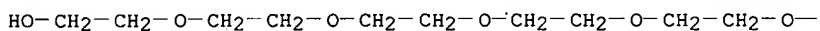


RN 19327-39-0 HCAPLUS  
CN 3,6,9,12-Tetraoxaeicosan-1-ol (6CI, 8CI, 9CI) (CA INDEX NAME)

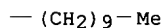


RN 23244-49-7 HCAPLUS  
CN 3,6,9,12,15-Pentaoxapentacosan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

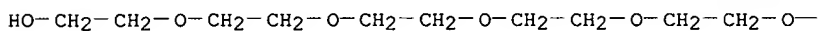


PAGE 1-B

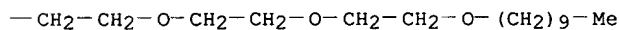


RN 24233-81-6 HCAPLUS  
CN 3,6,9,12,15,18,21,24-Octaoxatetratriacontan-1-ol (8CI, 9CI) (CA INDEX NAME)

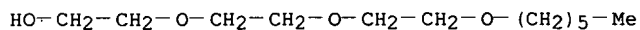
PAGE 1-A



PAGE 1-B

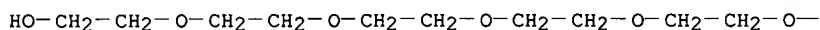


RN 25961-89-1 HCAPLUS  
CN Ethanol, 2-[2-[2-(hexyloxy)ethoxy]ethoxy]- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

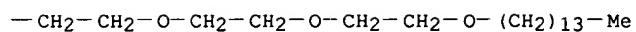


RN 27847-86-5 HCAPLUS  
CN 3,6,9,12,15,18,21,24-Octaoxaoctatriacontan-1-ol (8CI, 9CI) (CA INDEX NAME)

PAGE 1-A



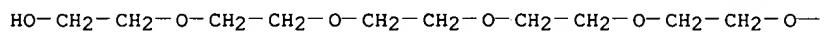
PAGE 1-B



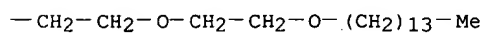
RN 40036-79-1 HCAPLUS

CN 3,6,9,12,15,18,21-Heptaoxapentatriacontan-1-ol (6CI, 9CI) (CA INDEX NAME)

PAGE 1-A



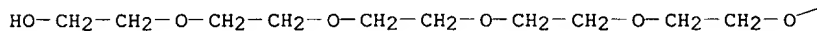
PAGE 1-B



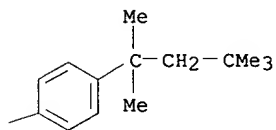
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L40 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1994:71539 HCAPLUS  
 DN 120:71539  
 TI Physical properties of silicone surfactants for agrochemical applications  
 AU Murphy, Dennis S.; Policello, George A.; Goddard, Errol D.; Stevens, Peter J. G.  
 CS Union Carbide Corp., Tarrytown, NY, 10591, USA  
 SO ASTM Spec. Tech. Publ. (1993), 1146(Pesticide Formulations and Applications Systems, 12th Vol.), 45-56  
 CODEN: ASTTA8; ISSN: 0066-0558  
 DT Journal  
 LA English  
 AB **Aq. solns.** of four silicone surfactants, and two hydrocarbon surfactants were studied over a range of concns. for dynamic surface tension lowering, spreading on paraffin wax film, and static surface tension. Dynamic surface tension profiles were obtained by both the oscillating jet method and the max. bubble pressure method. It was found that **aq. solns.** of the silicone surfactants lower surface tension more quickly, spread better on paraffin wax film, and yielded lower static surface tension values than corresponding **aq. solns.** of the hydrocarbon surfactants. Implications of the findings as regards effectiveness of these **adjuvants** are discussed.  
 IT 2315-64-2  
 RL: PRP (Properties)  
 (phys. properties of, silicone surfactants for agrochem. applications in relation to)  
 RN 2315-64-2 HCAPLUS  
 CN 3,6,9,12-Tetraoxatetradecan-1-ol, 14-[4-(1,1,3,3-tetramethylbutyl)phenoxy]-(9CI) (CA INDEX NAME)

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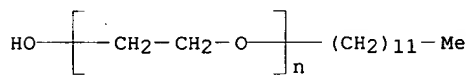
PAGE 1-B



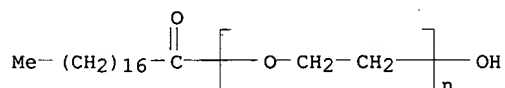
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L40 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1991:519977 HCAPLUS  
 DN 115:119977  
 TI Enhancing properties of surfactants on the release of carbamazepine from suppositories  
 AU Fontan, J. E.; Arnaud, P.; Chaumeil, J. C.  
 CS Dep. Pharmacotech., Fac. Sci. Pharm. Biol., Paris, 75270, Fr.  
 SO Int. J. Pharm. (1991), 73(1), 17-21  
 CODEN: IJPHDE; ISSN: 0378-5173  
 DT Journal  
 LA English  
 AB The effect of surfactants on physicochem. properties and on the release characteristics of carbamazepine from fatty suppositories was investigated in vitro. Four surfactants, polyoxyethylene 50-stearate (Simulsol M), polyoxyethylene 23-lauryl ether (Brij 35), and polysorbates 20 and 80, were examd. as **adjuvants**. The dissoln. rate was enhanced by all surfactants used. The dissoln. rate at 30 min increased from 54% without surfactant, to 100% with polysorbate 80 (2%). The liquefaction time could be the limiting factor for the dissoln. rate of carbamazepine. The better solubilizing effect of polysorbate 80 can be due to the better incorporation capacity of its **micelle**.  
 IT 9002-92-0, Brij 35 9004-99-3, Simulsol M  
 RL: BIOL (Biological study)  
 (carbamazepine release from suppositories enhancement by)  
 RN 9002-92-0 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)

*See above*



RN 9004-99-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)

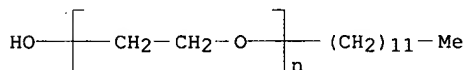


=&gt; d bib abs hitstr 4

L40 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1990:434374 HCAPLUS  
 DN 113:34374  
 TI Solubilization of unconjugated bilirubin and its calcium salts by ionic, amphoteric, and nonionic detergents  
 AU Wosiewicz, U.; Leuschner, U.  
 CS Abt. Gastroenterol., Universitaetsklin., Zent. Inneren Med., Frankfurt, D-6000, Fed. Rep. Ger.  
 SO Naturwissenschaften (1990), 77(5), 232-4  
 CODEN: NATWAY; ISSN: 0028-1042  
 DT Journal  
 LA English  
 AB Bile salts (BS) have been used as **adjuvants** in local chemolysis of pigment gallstones (PS), because these anionic detergents were found to solubilize unconjugated bilirubin (UCB), an obligatory product of PS chemolysis, and even its calcium salts, the main constituents of human PS. Since local chemolitholysis takes too much time in many cases, current irrigation media have to be improved. One of the possible approaches could be the substitution of the BS by another detergent with a higher solubilization efficiency for UCB and calcium bilirubinate. The soly. of UCB crystals as well as of amorphous CaB/Ca(BH)<sub>2</sub> depended on the surrounding pH and on the kind of detergent used. The highest (apparent) solubilities of UCB were found with nonionic (but polar), the lowest with anionic detergents, namely, with SDS. The considerable net (neg.) charge of the latter (more than 60 mols. per **micelle**) perhaps gives rise to repulsive forces which cause a decrease in soly. From the effects of the cationic hexadecyltrimethylammonium bromide it seems very likely that the elec. net charges of the detergents, which for their part are influenced by the pH, play an important role in the solubilization of UCB and its Ca salts. The results obtained in vitro suggest that improvement of local chemolysis of pigment material is possible in vivo, if nontoxic detergents are available with a greater solubilization efficacy than BS.

IT 9002-92-0  
 RL: BIOL (Biological study)  
 (gallstone pigment materials solubilization by, elec. charge in relation to)

RN 9002-92-0 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 5

L40 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1989:548771 HCAPLUS  
 DN 111:148771  
 TI Foliar absorption of some nonionic surfactants from **aqueous solutions** in the absence and presence of pesticidal active ingredients  
 AU Silcox, Dawn; Holloway, Peter J.  
 CS Agric. Prod. Res. Dev., Dow Chem., Wantage, UK  
 SO Adjuvants Agrochem. (1989), Volume 1, 115-28. Editor(s): Chow, Paul N. P.  
 Publisher: CRC, Boca Raton, Fla.  
 CODEN: 56OMA9  
 DT Conference  
 LA English  
 AB Foliar uptake expts. with 14C-labeled linear alcs. (C12E8, C13E6, C18E8.5) and alkylphenol poloxyethylene surfactants (OPE7, OPE9.5, NPE5.5, NPE9.5) demonstrated that considerable quantities of such compds. can enter plants following droplet applications of dil. **aq. solns.** The rates and total amts. of uptake varied greatly according to plant species, and both were influenced by the chem. nature of the surfactant. The surfactants examd. had hydrophile-lipophile balance (HLB) values in the range 10 to 14, and max. foliar absorption was obsd. for compds. having a C12/C13 alkyl chain as the hydrophobic moiety. There was little movement of any of the surfactants following penetration into leaves, but they were subsequently metabolized within the treated areas, the rate and products of metab. again differing with plant species. On Vicia faba leaves, surfactant uptake was altered greatly in the presence of a no. of different water-sol. agrochems., anionic compds. slowing absorption to a greater extent than cationic ones. The intimate relationship between surfactant and chem. during foliar penetration was confirmed by further expts. on the same plant with the 14C-labeled herbicide difenzoquat. The implications of the findings in terms of elucidating the possible mode of action of surfactants as spray **adjuvants** are discussed.  
 IT 930-09-6, 3,6,9,12,15,18-Hexaoxahentriacontan-1-ol  
 3055-98-9 9002-93-1 9005-00-9  
 26027-38-3  
 RL: PROC (Process)  
 (foliar absorption of, in presence or absence of pesticides)  
 RN 930-09-6 HCAPLUS  
 CN 3,6,9,12,15,18-Hexaoxahentriacontan-1-ol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

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HO-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-

PAGE 1-B

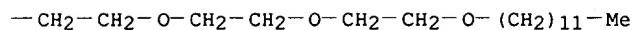
-CH<sub>2</sub>-CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>12</sub>-Me

RN 3055-98-9 HCAPLUS  
 CN 3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI) (CA INDEX NAME)

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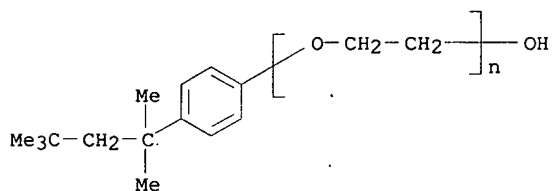
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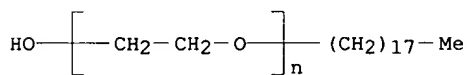
RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-  
.omega.-hydroxy- (9CI) (CA INDEX NAME)



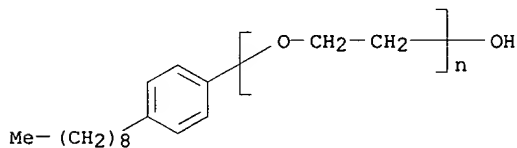
RN 9005-00-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA  
INDEX NAME)



RN 26027-38-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
(CA INDEX NAME)



=&gt; d bib abs hitstr 6

L40 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1987:483791 HCAPLUS

DN 107:83791

TI Effects of sodium taurodihydrofusidate on nasal absorption of insulin in sheep

AU Longenecker, John P.; Moses, Alan C.; Flier, Jeffrey S.; Silver, Robert D.; Carey, Martin C.; Dubovi, Edward J.

CS California Biotechnol., Inc., Mt. View, CA, 94134, USA

SO J. Pharm. Sci. (1987), 76(5), 351-5

CODEN: JPMSAE; ISSN: 0022-3549

DT Journal

LA English

AB To investigate the utility of a novel **adjuvant**, Na taurodihydrofusidate (STDHF), as an enhancer of mucosal permeation of drugs, expts. involving ~~intranasal~~ insulin-STDHF administration in sheep were performed. Rabbit erythrocyte lysis assays were employed to assess the relative membrane lytic activity of STDHF, as well as that of its glycine-conjugated analog, compared with a nonionic detergent and a common bile salt. Equiv. wt. concns. of the fusidates were 5- to 10-fold less lytic than the bile salt and at least 100-fold less lytic than the nonionic detergent laureth-9. Provided the concn. of STDHF was greater than its crit. **micellar** concn., formulations of insulin with STDHF greatly enhanced intranasal insulin absorption. Optimal nasal insulin absorption was attained at a molar ratio of STDHF to insulin of 5:1. In addn., intranasal absorption was linearly related to insulin dose. Compared with i.v. administration, the mean bioavailability of intranasal insulin was 16.4%. Interovine variability was low, with a coeff. of variation of 14% for 12 animals. Intranasal absorption of Na insulin was not significantly different from that of Zn insulin. However, formulations of both cryst. insulin preps. were absorbed more efficiently than a formulation prepd. using com. available solns. of U-500 insulin. The results taken together indicate that STDHF is an excellent enhancer of insulin absorption from the nasal mucosa.

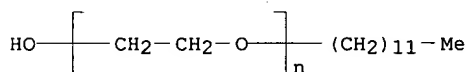
IT 9002-92-0, Laureth 9

RL: BIOL (Biological study)

(insulin intranasal absorption enhancement by taurodihydrofusidate in relation to)

RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)





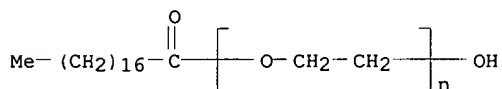
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L40 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1986:193210 HCAPLUS  
 DN 104:193210  
 TI Erodible matrix for sustained release bioactive composition  
 IN Snipes, Wallace C.  
 PA Zetachron, Inc., USA  
 SO PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8600802	A1	19860213	WO 1985-US1349	19850717
	W: AU, JP, KP				
	RW: BE, CH, DE, FR, GB, NL				
	CA 1246448	A1	19881213	CA 1985-486711	19850712
	AU 8546388	A1	19860225	AU 1985-46388	19850717
	AU 573149	B2	19880526		
	EP 190255	A1	19860813	EP 1985-903908	19850717
	EP 190255	B1	19921111		
	R: BE, CH, DE, FR, GB, LI, NL				
	JP 61502759	T2	19861127	JP 1985-503436	19850717
PRAI	US 1984-633604		19840723		
	WO 1985-US1349		19850717		

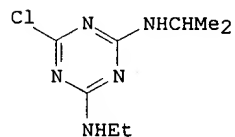
AB A sustained-release oral compn. erodable in aq. soln.  
 comprises 5-95% by wt. of PEG (mol. wt. 1000-20,000) and 95-5% of an  
 erosion rate modifier (e.g., fatty acid) which is amphiphilic and insol.  
 in the aq. soln. Thus, compns. contg. PEGs 1000,  
 4000, 8000, or 20,000 (37.5% each), myristic acid 15%, starch (22.5%), and  
 indomethacin 25% all released the drug gradually over a period of several  
 h.

IT 9004-99-3  
 RL: BIOL (Biological study)  
 (sustained-release erodable matrix pharmaceutical compns. manuf. with)  
 RN 9004-99-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



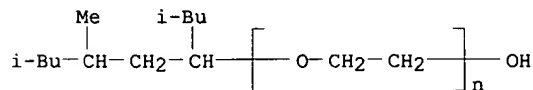
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L40 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1984:169856 HCAPLUS  
 DN 100:169856  
 TI Surface tension and contact angle of herbicide solutions affected by surfactants  
 AU Singh, Megh; Orsenigo, J. R.; Shah, D. O.  
 CS Inst. Food Agric. Sci., Univ. Florida, Lake Alfred, FL, 33850, USA  
 SO JAOCs, J. Am. Oil Chem. Soc. (1984), 61(3), 596-600  
 CODEN: JJASDH  
 DT Journal  
 LA English  
 GI



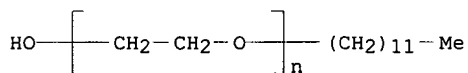
AB Contact angle and surface tension were measured for distd. H<sub>2</sub>O and hard water solns. of **adjuvants** Ortho X-77 [12687-90-0], Span-20 [1338-39-2], Sterox-NJ [59644-67-6], Surfactant-WK [60828-78-6], Triton B-1956, Triton X-114 [9036-19-5], Tween-20 [9005-64-5], and Sun Oil 11E. The same parameters were measured for suspensions of atrazine (I) [1912-24-9] and ametryn [834-12-8] with and without each **adjuvant**. All **adjuvants** reduced surface tension and contact angle of H<sub>2</sub>O; surfactant-WK was most effective and Tween-20 was least effective. Increasing concn. of surfactants from 0 to 0.1% (vol./vol.) gave progressive redn. in surface tension and contact angle, whereas higher concns., 0.1-2.0% (vol./vol.), had no further effect. Surfactant-WK at 0.1% in H<sub>2</sub>O reduced surface tension from 72.8 to 27 dynes/cm and contact angle from 110.degree. to 41.degree.. An addnl. increase in Surfactant-WK concn. from 0.1 to 2% did not further reduce surface tension and contact angle. Sun Oil 11E was identical in behavior except that it was less effective than the surfactants. Water hardness .1to req. 1000 ppm as Ca<sup>2+</sup> did not affect surface tension and contact angle in surfactant solns. An **aq. soln.** of I had a higher surface tension and contact angle than ametryn in the absence of surfactants. However, these differences were not obsd. when surfactants were added to either herbicide.

IT 60828-78-6  
 RL: BIOL (Biological study)  
 (contact angle and surface tension of herbicide solns. contg.)  
 RN 60828-78-6 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[3,5-dimethyl-1-(2-methylpropyl)hexyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 9

L40 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1983:95551 HCAPLUS  
 DN 98:95551  
 TI Vaginal absorption of a potent luteinizing hormone-releasing hormone analog (leuprolide) in rats. I: Absorption by various routes and absorption enhancement  
 AU Okada, Hiroaki; Yamazaki, Iwao; Ogawa, Yasuaki; Hirai, Shinichiro; Yashiki, Takatsuka; Mima, Hiroyuki  
 CS Cent. Res. Div., Takeda Chem. Ind., Ltd., Yodogawa, 532, Japan  
 SO J. Pharm. Sci. (1982), 71(12), 1367-71  
 CODEN: JPMSAE; ISSN: 0022-3549  
 DT Journal  
 LA English  
 AB The absorption of leuprolide [53714-56-0] by different routes was evaluated by detg. the ovulation-inducing activity in diestrous rats. Vaginal administration showed the greatest potency among nonparenteral routes and was followed successively by rectal, nasal, and oral administration. A mixed micellar soln. with monoolein [25496-72-4]-bile acids improved the intestinal absorption of leuprolide, and nasal absorption was enhanced by adding Na glycocholate [863-57-0], surfactin [24730-31-2], or polyoxyethylene 9 lauryl ether [9002-92-0], but these bioavailabilities were still insufficient. The vaginal absorption was enhanced by citric acid [77-92-9], succinic acid [110-15-6], tartaric acid [87-69-4], and glycocholic acid [475-31-0]; the abs. bioavailability increased to .apprx.20%. The vaginal absorption from jellies, as practical dosage forms, yielded sufficient activity of leuprolide, but absorption was slightly reduced with highly polar polymers or with higher concns. of polymers. Vaginal administration of leuprolide can be a rational dosage method for long-term antitumor therapy.  
 IT 9002-92-0  
 RL: BIOL (Biological study)  
 (leuprolide absorption by nose and vagina increase by)  
 RN 9002-92-0 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 10

L40 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1973:47733 HCAPLUS

DN 78:47733

TI Influence of auxiliary material on pharmaceuticals. 21. Mechanism of interaction between esters of nicotinic acid and poly(oxyethylene) ethers

AU Ullmann, E.; Thoma, K.; Lippold, B. C.

CS Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger.

SO Arch. Pharm. (Weinheim, Ger.) (1972), 305(11), 797-802

CODEN: ARPMAS

DT Journal

LA German

AB The interactions between surface-active poly(oxyethylene) ethers and esters of nicotinic acid take place in the hydrophobic interior and in the hydrophilic exterior of the **micelles**. The degree of binding of the esters to the **micelles** depends particularly on the physicochem. properties of the esters. The lipophilic hexyl ester, e.g., is bound to a much greater extent than the hydrophilic Et ester. The structure of the surface-active agents has only a small effect. From the exptl. results, conclusions are drawn about the localization of the esters in the **micelles**.

IT 9002-92-0 9004-95-9 9005-00-9

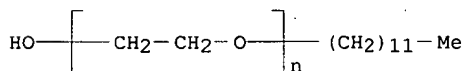
27306-79-2

RL: BIOL (Biological study)

(pharmaceutical **adjuvants**, nicotinate reaction with)

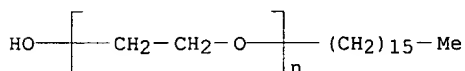
RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



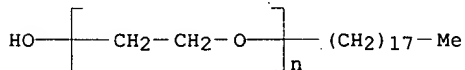
RN 9004-95-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



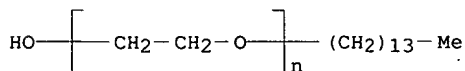
RN 9005-00-9 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



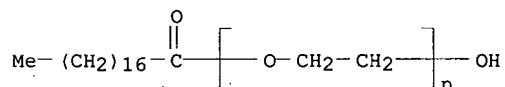
RN 27306-79-2 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-tetradecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



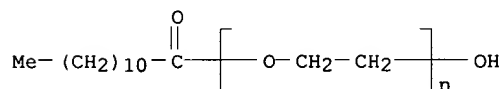
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L40 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1968:509780 HCAPLUS  
 DN 69:109780  
 TI Effect of **adjuvants** in the preparation of pharmaceuticals. XIX.  
 Effect of surfactants on ester hydrolysis  
 AU Ullmann, Elsa; Thoma, K.; Rombach, R.  
 CS Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Ger.  
 SO Arch. Pharm. (Weinheim) (1968), 301(5), 363-9  
 CODEN: APBDAJ  
 DT Journal  
 LA German  
 AB The stabilization of phenyl salicylate (I) by surfactants was detd. I  
 hydrolyzed completely in **aq. soln.** at pH 7 and  
 20.degree. in 30 days. It was stabilized completely by 0.5% Na lauryl  
 sulfate, but not by 0.5% cetyltrimethylammonium bromide. In MeOH soln. I  
 was stabilized for 5 days by 2% polyethylene glycol 1000, but not  
 completely by 0.5% polyethylene glycol 900 sorbitan monooleate. In the  
 presence of 5% polyethylene glycol 1400 stearate, the decompn. rate of I  
 increased with temp.  
 IT 9004-99-3  
 RL: BIOL (Biological study)  
 (phenyl salicylate stability in relation to)  
 RN 9004-99-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



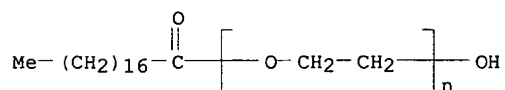
=&gt; d bib abs hitstr 12

L40 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1968:418088 HCAPLUS  
 DN 69:18088  
 TI Food additives. Sanitizing solutions  
 AU Anon.  
 SO Fed. Regist. (1968), 33, 7684, 24 May 1968  
 CODEN: FEREAC  
 DT Journal  
 LA English  
 AB An **aq. soln.** of I, butoxy monoether of mixed  
 (ethylene-propylene) polyalkylene glycol with min. av. mol. wt. of 2400,  
 and .alpha.-lauroyl-.omega.-hydroxypoly(oxyethylene) with an av. of 8-9  
 moles of ethylene oxide and an av. mol. wt. of 400, together with  
**adjuvants** may be used under the Federal Food, Drug, and Cosmetic  
 Act as a sanitizing soln. on food processing equipment and utensils that  
 contact food and on beverage containers except those used for milk. The  
 soln. must contain 25 ppm. titratable I.  
 IT **9004-81-3**  
 RL: BIOL (Biological study)  
 (sanitizing solns. contg., standards for)  
 RN 9004-81-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxododecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



=&gt; d bib abs hitstr 13

L40 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1967:405685 HCAPLUS  
 DN 67:5685  
 TI Effect of **adjuvants** on drug preparations. XVI. The effect of the hydrophilic-lipophilic equilibrium (HLB-value) of surfactants on the release and activity of antibacterial compounds  
 AU Thoma, Karl  
 CS Univ. Munich, Munich, Ger.  
 SO Arch. Pharm. Ber. Dtsch. Pharm. Ges. (1967), 300(1), 31-8  
 CODEN: APBDAJ  
 DT Journal  
 LA German  
 AB cf. CA 66: 98459s. The effect of nonionized surfactants on antiseptic ointments, solns., and preservatives was studied. No significant relation was found between HLB values and the influence of the compd. on the activity of (.beta.-phenoxyethyl)dimethyldodecylammonium bromide (I), 1-hexadecylpyridinium chloride (II), di-Na 2,7-dibromo-4-(hydroxymercuri)fluorescein (III), and Na methylmercurithiosalicylate (IV). The addn. of ethers of polyethylene glycols (PEG), PEG 250 lauryl ether (V), PEG 900 stearyl ether (VI), PEG 1400 stearyl ether (VII) to I and III in ointments and solns. reduced the antibacterial activity of I and III against *Staphylococcus aureus* SG 511. The invert soaps, PEG sorbitan monolaurate (VIII), PEG sorbitan stearate (IX), PEG sorbitan trioleate (X), PEG 400 stearate (XI), PEG 900 stearate (XII), and PEG 2200 stearate (XIII) produced a very strong decrease in availability of I in ointments and **aq. solns.** The availability of III in ointments was reduced by VIII-XIII but **aq. solns.** of III were unaffected. The diffusion of I and III was not dependent on the HLB value of the additive. The bactericidal activity of II was changed by less than 1% XII so that II was bacteriostatic; bacteriostatic activity was lost above 5% XII. V, VIII, and sucrose monolaurate (XIV) acted similarly. IV was unaffected by V-XIII. The effects of V-XIII are not due to their structure (PEG 1000 is indifferent towards invert soaps but is strongly impaired by XIV) but is caused by the existence of a 2nd pseudophase in the form of **micelles** of surfactant.  
 IT 9004-99-3  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
 (antibiotic activity response to)  
 RN 9004-99-3 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



IT 32127-87-0  
 RL: BIOL (Biological study)  
 (bactericidal activity of ointments and)  
 RN 32127-87-0 HCAPLUS

CEPERLEY 09/647,518

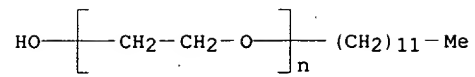
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L47 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:355059 HCAPLUS  
 DN 134:357576  
 TI Preparation of mixed micellar delivery system for pharmaceutical proteins  
 IN Modi, Pankaj  
 PA Generex Pharmaceuticals Inc., Can.  
 SO U.S., 13 pp., Cont.-in-part of U.S. Ser. No. 21,114.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6231882	B1	20010515	US 1998-216733	19981221
	US 6017545	A	20000125	US 1998-21114	19980210
	BR 9804295	A	20000328	BR 1998-4295	19981027
	WO 9940932	A1	19990819	WO 1999-CA106	19990205
	W:		AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	AU 9925053	A1	19990830	AU 1999-25053	19990205
	EP 1053011	A1	20001122	EP 1999-904638	19990205
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
	US 6221378	B1	20010424	US 1999-386285	19990831
PRAI	US 1998-21114	A2	19980210		
	US 1998-216733	A	19981221		
	WO 1999-CA106	W	19990205		
AB	A mixed micellar pharmaceutical formulation includes (1) a micellar proteinic pharmaceutical agent, i.e., heparin, hirulog, hirudin, interferons, interleukins, cytokines, and polyclonal antibodies, chemotherapeutic agents, glycoproteins, bacterial toxoids, hormones, antibiotics, platelet inhibitors, DNA, RNA, antisense oligonucleotides, steroids, hypnotics, and pain killers, e.t.c., (2) an alkali metal C8-22 alkyl sulfate, (3) alkali metal salicylate, (4) a pharmaceutically acceptable edetate and (5) at least one absorption enhancing compds. The absorption enhancing compds. are selected from the group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile ext., cucumber ext., oleic acid, linolenic acid, borage oil, evening primrose oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin, lysine, polylysine, triolein and mixts. thereof. The amt. of each absorption enhancing compd. is present in a concn. of 1-10% by wt. of the total formulation, and the total concn. of absorption enhancing compds. are < 50% by wt. of the formulation. For example, a micellar insulin soln. was prepd. using 0.5 g sodium lauryl sulfate, 0.5 g Na salicylate, and 0.25 g disodium edetate dissolved in 10 mL of water. To this soln. 40 mg (1000 units) of insulin was added and dissolved completely while stirring, to give about 100 units/mL insulin oral soln. Compared to the injections, oral insulin gave a faster onset of action and lowered blood glucose levels without creating hypoglycemic condition. Due to the hepatic glucose prodn., there was a rebound effect. This is believed to be due to the incomplete absorption of insulin.				
IT	9002-92-0D, Polydocanol, alkyl ethers RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of mixed micellar delivery system for proteinic drugs)				
RN	9002-92-0 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



CEPERLEY 09/647,518



RE.CNT 1

RE

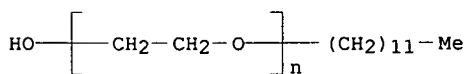
(1) Modi; US 6017545 2000 HCAPLUS

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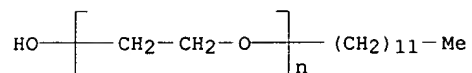
L47 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:167782 HCAPLUS  
 DN 134:227361  
 TI Preparation of mixed micellar pharmaceutical delivery system for  
 proteinic and other drugs  
 IN Modi, Pankaj  
 PA Generex Pharmaceuticals Inc., Can.  
 SO PCT Int. Appl., 46 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001015666	A1	20010308	WO 2000-CA1019	20000825
	W:		AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:		GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	US 6221378	B1	20010424	US 1999-386285	19990831
PRAI	US 1999-386285	A	19990831		
	US 1998-21114	A2	19980210		
	US 1998-216733	A2	19981221		
AB	A mixed micellar pharmaceutical formulation and process for making the formulation are described. The formulation includes a micellar proteinic pharmaceutical agent, an alkali metal C8-22 alkyl sulfate, alkali metal salicylate, a pharmaceutically acceptable edetate and at least one absorption enhancing compd. The absorption enhancing compd. is selected from the group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile ext., cucumber ext., oleic acid, linolenic acid, borage oil, evening primrose oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin, lysine, polylysine, triolein and mixts. thereof. The amt. of each absorption enhancing compd. is present in a concn. of 1-10% by wt.; the total formulation, and the total concn. of absorption enhancing compds. are < 50% by wt. of the formulation. Preferably, the formulation is administered, in combination with a propellant, to the buccal cavity, using a metered dose dispenser, which is also described. For example, an oral drops were prepd. using 0.5 g sodium lauryl sulfate, 0.5 g sodium salicylate and 0.25 g disodium edetate dissolved in 10 mL of water. To this soln. 40 mg (1000 units) of insulin was added and dissolved completely while stirring, to give about 100 units/mL insulin soln. Compared to the injection method, oral insulin gives a faster onset of action and lowers blood glucose levels without creating hypoglycemic condition. Due to the hepatic glucose prodn., there was a rebound effect. This is believed to be due to the incomplete absorption of insulin.				
IT	9002-92-0, Polyoxyethylene lauryl ether 9002-92-0D, Polydocanol, alkyl ethers RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of mixed micelles for oral delivery of proteinic and other drugs)				
RN	9002-92-0 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)				

*see above*



RN 9002-92-0 HCAPLUS  
CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA  
INDEX NAME)



RE.CNT 6

RE

- (1) Astra Ab; WO 9619197 A 1996 HCAPLUS
  - (2) Genentech Inc; WO 9426302 A 1994 HCAPLUS
  - (3) Genex Pharm Inc; WO 0037051 A 2000 HCAPLUS
  - (4) Modi, P; WO 9636352 A 1996 HCAPLUS
  - (5) Modi, P; WO 9940932 A 1999 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d bib abs hitstr 3

L47 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2001:63806 HCAPLUS  
 DN 134:136684  
 TI Biodegradable poly(alkylene oxide)-poly(p-dioxanone) block copolymer  
 soluble in organic solvents, and drug delivery composition comprising same  
 IN Seo, Min-Hyo; Choi, In-Ja  
 PA Samyang Corporation, S. Korea  
 SO PCT Int. Appl., 35 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

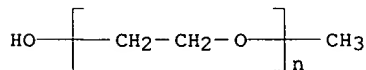
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005379	A1	20010125	WO 2000-KR779	20000718
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI KR 1999-29269	A	19990720		
AB The present invention relates to a biocompatible and biodegradable block copolymer of poly(alkylene oxide) and poly(p-dioxanone) (PDO), which is sol. in org. solvents, for delivery of peptides, proteins, antitumor agents, antiphlogistic anodyne agents, antibiotics, antibacterials, hormones, genes, and <b>vaccines</b> . Drug delivery compns. comprise microspheres, microcapsules, films, strips, fibers, gels, sols, nanospheres, nanocapsules, and <b>micelles</b> . For example, 5 g of poly(ethylene glycol) monomethyl ether and 10 g of 1,4-dioxane-2-one reacted in presence of 4.06 mg of stannous octoate to obtain a mPEG-PDO diblock copolymer with the mPEG content of 46.3 wt.%. The mPEG-PDO diblock copolymer (0.85 g) was dissolved in 2 mL of dichloromethane and 0.15 g of ofloxacin was suspended therein. The suspension was added to a 1 wt.% polyvinyl alc. <b>aq. soln.</b> and stirred at 1200 rpm to obtain a microsphere soln. The soln. was freeze-dried to give microspheres having an av. particle size of 10 .mu. and contg. 14.6% ofloxacin.				
IT 321658-19-9P RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (diblock; biodegradable poly(alkylene oxide)-poly(p-dioxanone) block copolymer sol. in org. solvents for drug delivery systems)				
RN 321658-19-9	HCAPLUS			
CN 1,4-Dioxan-2-one, polymer with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2- ethanediyl), block (9CI) (CA INDEX NAME)				

CM 1

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O

CCI PMS

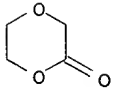


CM 2

CRN 3041-16-5

CMF C4 H6 O3

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RE.CNT 2

RE

(1) Ethicon; US 5019094 1991 HCAPLUS

(2) United States Surgical Corp; US 5522841 1996 HCAPLUS

=&gt; d bib abs hitstr 4

L47 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:741894 HCAPLUS  
 DN 133:313641  
 TI Lipid aggregate-forming compositions and their uses  
 IN Leigh, Steven; Leigh, Mathew Louis Steven  
 PA Phares Pharmaceuticals Research N.V., Neth. Antilles  
 SO PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061113	A1	20001019	WO 2000-GB1361	20000411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI GB 1999-8309	A	19990412		
AB Formulations are provided which contain at least one <b>micelle</b> -forming monoacyl membrane lipid either alone or preferably in combination with one or more bilayer-forming diacyl membrane lipids. The compns. are characterized by the presence of an effective amt. of the monoacyl component and a lipophilic component dissolved or dispersed in a hydrophilic medium in an amt. effective to convert the compn. into a liq., gel or semi-solid which has the property of yielding dispersed lipid aggregates upon contact or further dildn. with an aq. medium. Particular liq. pharmaceutical compns. comprise: (a) a mixt. of membrane lipids which comprises a <b>micelle</b> -forming lipid and preferably a bilayer-forming lipid; (b) a lipophilic component; (c) at least one hydrophilic medium to mobilize the lipids; and optionally (d) a biol. active compd. Other compns. comprise water in an amt. which is effective to hydrate the lipid mixt., and a biol. active compd. Enzyme modified lecithin 40, Miglyol 810 10, vitamin A propionate 5 parts were dissolved in ethanol 20, propylene glycol 10, and water 5. The compn. was heated and dild. to obtain a clear yellow dispersion of microscopic lipid aggregates.				
IT 111-90-0 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (drug carriers contg. <b>micelle</b> -forming membrane lipids and bilayer-forming lipids and other ingredients)				
RN 111-90-0 HCAPLUS				
CN Ethanol, 2-(2-ethoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)				

$$\text{EtO}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{OH}$$

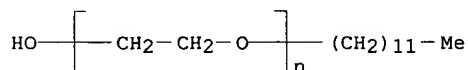
RE.CNT 5  
 RE

- (1) Cipla Limited; EP 0760237 A 1997 HCAPLUS
- (2) Hoechst Ag; EP 0649660 A 1995 HCAPLUS
- (3) Leigh, M; WO 9858629 A 1998 HCAPLUS
- (4) Leigh, M; WO 9944642 A 1999 HCAPLUS
- (5) Vesifact Ag; EP 0956853 A 1999 HCAPLUS

=&gt; d bib abs hitstr 5

L47 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 2000:441602 HCAPLUS  
 DN 133:63985  
 TI Aerosol formulations for buccal and pulmonary application  
 IN Modi, Pankaj  
 PA Generex Pharmaceuticals Inc., Can.  
 SO PCT Int. Appl., 46 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037051	A1	20000629	WO 1999-CA1231	19991216
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1998-113239	P	19981221		
	US 1999-251464	A	19990217		
	US 1999-386284	A	19990831		
AB	A mixed <b>micellar</b> aerosol pharmaceutical formulation includes a <b>micellar</b> protein pharmaceutical agent, an alkali metal lauryl sulfate, at least three <b>micelle</b> forming compds., a phenol and a propellant. The <b>micelle</b> forming compds. are selected from the group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, glycolic acid, lactic acid, chamomile ext., cucumber ext., oleic acid, linoleic acid, linolenic acid, monoolein, monooleates, monolaurates, borage oil, evening of primrose oil, menthol, trihydroxy oxocholanyl glycine and pharmaceutically acceptable salts thereof, glycerin, polyglycerin, lysine, polylysine, triolein, polyoxyethylene ethers and analogs thereof, polydocanol alkyl ethers and analogs thereof, chenodeoxycholate and deoxycholate. The amt. of each <b>micelle</b> forming compd. is present in a concn. of from 1 to 20 wt./wt.% of the total formulation, and the total concn. of <b>micelle</b> forming compds. are less than 50 wt./wt.% of the formulation. The propellant, e.g., a fluorocarbon propellant, provides enhanced absorption of the pharmaceutical agent, particularly in the buccal cavity. An example was given using insulin as the active ingredient.				
IT	9002-92-0				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (aerosol formulations for buccal and pulmonary application)				
RN	9002-92-0 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



RE.CNT 6

RE

- (1) Alliance Pharma; WO 9640057 A 1996 HCAPLUS
  - (2) Biozone Lab Inc; WO 9742938 A 1997 HCAPLUS
  - (3) Chandarana, S; WO 9636352 A 1996 HCAPLUS
  - (4) Leigh, S; US 5004611 A 1991 HCAPLUS
  - (5) Modi, P; WO 9940932 A 1999 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

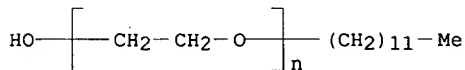
CEPERLEY 09/647,518



=&gt; d bib abs hitstr 6

L47 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:795833 HCAPLUS  
 DN 132:26803  
 TI Method for preparing virus-safe pharmaceutical compositions  
 IN Tolo, Hannele; Parkkinen, Jaakko  
 PA Suomen Punainen Risti Veripalvelu, Finland  
 SO PCT Int. Appl., 23 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964441	A1	19991216	WO 1999-FI505	19990609
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FI 9801337	A	19991211	FI 1998-1337	19980610
AU 9947834	A1	19991230	AU 1999-47834	19990609
EP 1086120	A1	20010328	EP 1999-931279	19990609
R: AT, CH, DE, ES, FR, GB, LI, NL, SE				
PRAI FI 1998-1337	A	19980610		
WO 1999-FI505	W	19990609		
AB The present invention concerns a method of prepg. pharmaceutical compns. of a biol. active proteins, in particular multicomponent interferon compns. The invention comprises the steps of adding to a soln. of the protein a non-ionic detergent in an efficient amt. to provide an extended shelf-life of the pharmaceutical compn.; subjecting the soln. contg. the nonionic detergent to filtration on a virus removal filter with a pore size of 10 to 40 nm; and recovering the filtrate. The method gives rise to, e.g., a virus-safe multicomponent .alpha.-interferon compn., comprising a nonionic detergent as a stabilizer in an amt. exceeding the crit. micellar concn. of the detergent and being essentially free from substances retained on a virus-filter having high virus retentive capacity.				
IT 9002-92-0, Brij 35 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (prepg. virus-safe pharmaceutical compns.)				
RN 9002-92-0 HCAPLUS				
CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



RE.CNT 3

RE

- (1) Dr Karl Thomas GmbH; EP 0231816 A2 1987 HCAPLUS
- (2) Interferon Sciences, Inc A Delaware Corporation; EP 0152345 A2 1985 HCAPLUS
- (3) Seitz-Filter-Werke GmbH Und Co; EP 0571871 A2 1993 HCAPLUS

=&gt; d bib abs hitstr 7

L47 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:686550 HCAPLUS  
 DN 131:303230  
 TI Customization of hair care formulations  
 IN Rath, Maureen L.; Hlavac, Wallace R.  
 PA Tiro Industries Incorporated, USA  
 SO U.S., 13 pp., Cont. of U.S. Ser. No. 969,492.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 2

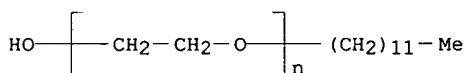
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5972322	A	19991026	US 1999-304246	19990503
	US 5993792	A	19991130	US 1997-969492	19971113
PRAI	US 1997-969492		19971113		

AB The invention provides a system for prepg. a hair shampoo, conditioner, and styling compn., wherein each system is composed of sep. components that can be combined as desired by the user to provide customized hair care formulations. The systems include a water-thin base compn., a thickening compn., and optional enhancing additives, wherein each compn. is sep. packaged. The viscosity of the end-product shampoo, conditioner, or styling compn. can be varied, from a thick, pourable liq. to a thicker, pasty material depending on the amt. of thickener that is added to the base. An optional styling compn. was prepd. by combining the ingredients shown below. The product contained deionized water 75.0, Germaben II 1.0, 20% aq. soln. of Gafquat 755N 8.0, and 50% aq. soln. of PVP/VA W-35 16.0%.

IT 9002-92-0, Laureth-23 9004-99-3D, C16-18- and iso-C16-18-alkyl ethers 24938-91-8, Salcare-SC95  
 RL: BUU (Biological use, unclassified); BIOL (Biological study);  
 USES (Uses)  
 (customization of hair care formulations)

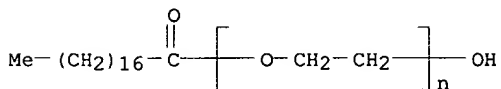
RN 9002-92-0 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



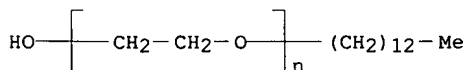
RN 9004-99-3 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 24938-91-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-tridecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 15

RE

(1) Anon; WO 9725963 1997 HCAPLUS

CEPERLEY 09/647,518

(2) Casperson; US 5376146 1994 HCAPLUS  
(3) Ciaudelli; US 5084270 1992 HCAPLUS  
(4) Darkwa; US 5077042 1991 HCAPLUS  
(5) Darkwa; US 5293885 1994 HCAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d bib abs hitstr 8

L47 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:655903 HCAPLUS  
 DN 131:285527  
 TI Manufacture of the pancreatic islet autoantigen GAD65 in methylotrophic yeasts  
 IN Raymond, Christopher K.; Bukowski, Thomas R.; Bishop, Paul D.  
 PA ZymoGenetics, Inc., USA  
 SO U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 703,807.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5965389	A	19991012	US 1996-747108	19961108
	US 5716808	A	19980210	US 1996-703809	19960826
	US 5955349	A	19990921	US 1996-703807	19960826
	CA 2237039	AA	19970515	CA 1996-2237039	19961108
	CA 2237120	AA	19970515	CA 1996-2237120	19961108
	US 5888768	A	19990330	US 1997-932924	19970918
PRAI	US 1995-6397	P	19951109		
	US 1996-703807	A2	19960826		
	US 1996-703809	A2	19960826		

AB A method of manufg. a biol. active form of the GAD65 autoantigen of pancreatic islets by expression of the gene in methylotrophic yeasts is described. The GAD65 autoantigen is a glutamate decarboxylase with several disulfide bridges and two palmitoylated sites that aggregates readily in aq. soln. A methanol-inducible promoter from, for example, an alc. oxidase gene, such as *Pichia pastoris* AOX1, can be used to regulate GAD65 expression. The GAD65 has high specific activity and retains **antigenic** characteristics of the native mol. that are essential to immunol. assays and therapeutic protocols. Development of a non-secretory expression system for *Pichia methanolica* using the promoters of alc. utilization genes (AUG1 and AUG2) and ADE2 auxotrophic marker is also described. Purifn. of the enzyme from producer strains using detergent phase sepn. with Triton X114 and ion-exchange chromatog. is also demonstrated.

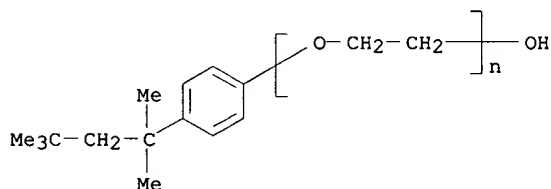
IT 9002-93-1, Triton X-100

RL: BUU (Biological use, unclassified); MOA (Modifier or additive use); BIOL (Biological study); USES (Uses)

(in solubilization and purifn. of GAD65; manuf. of pancreatic islet autoantigen GAD65 in methylotrophic yeasts)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 29

RE

- (1) Anon; EP 0299108 1989 HCAPLUS
- (2) Anon; EP 0341746 1989 HCAPLUS
- (3) Anon; WO 92/05446 1992 HCAPLUS
- (4) Anon; WO 92/20811 1992 HCAPLUS
- (5) Anon; WO 95/04137 1995 HCAPLUS

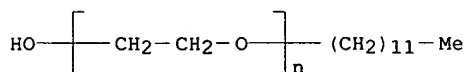
ALL CITATIONS AVAILABLE IN THE RE FORMAT

CEPERLEY 09/647,518

=&gt; d bib abs hitstr 9

L47 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1999:529037 HCAPLUS  
 DN 131:161639  
 TI Mixed **micellar** pharmaceutical delivery system containing  
 proteins  
 IN Modi, Pankaj  
 PA Can.  
 SO PCT Int. Appl., 55 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9940932	A1	19990819	WO 1999-CA106	19990205
	W:		AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	US 6017545	A	20000125	US 1998-21114	19980210
	US 6231882	B1	20010515	US 1998-216733	19981221
	AU 9925053	A1	19990830	AU 1999-25053	19990205
	EP 1053011	A1	20001122	EP 1999-904638	19990205
	R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
PRAI	US 1998-21114	A	19980210		
	US 1998-216733	A	19981221		
	WO 1999-CA106	W	19990205		
AB	A mixed <b>micellar</b> pharmaceutical formulation includes a <b>micellar</b> proteinic pharmaceutical agent, an alkali metal C8-22 alkyl sulfate, alkali metal salicylate, a pharmaceutically acceptable edetate and at least one absorption enhancing compds. The absorption enhancing compds. are selected from the group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile ext., cucumber ext., oleic acid, linolenic acid, borage oil, evening primrose oil, trihydroxy oxo cholanylglycine, glycerin, polyglycerin, lysine, polylysine, triolein and mixts. thereof. The amt. of each absorption enhancing compd. is present in a concn. of from 1 to 10 wt./wt.% of the total formulation, and the total concn. of absorption enhancing compds. are less than 50 wt./wt.% of the formulation. Insulin was added to a buffer soln. contg. sodium lauryl sulfate 0.5, sodium salicylate 0.5, disodium edetate 0.25 g, and water 10 mL and mixed to form <b>micellar</b> insulin. To a soln. of 100 mg phosphatidylcholine-H in 10 mL 50% ethanol was added 16 mg (400 units) of <b>micellar</b> insulin soln. To this was added 0.6 mL of sodium hyaluronate and 0.2 mL of 2% menthol soln. contg. 3% sorbitol. Type II diabetic human volunteers were given 30 units (about 20 drops) of the above oral soln. (3 times the injection dose). The oral insulin formulation was comparable to the injected insulin in lowering blood glucose level.				
IT	9002-92-0, Polidocanol				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
	(mixed <b>micellar</b> pharmaceutical delivery system contg. proteins)				
RN	9002-92-0 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)				

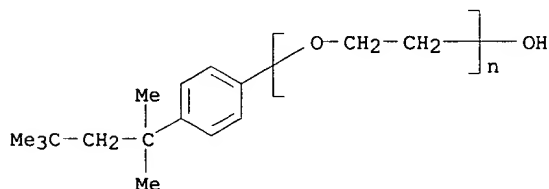


RE.CNT 4

RE

- (1) Baeckstroem, K; WO 9619197 A 1996 HCAPLUS
- (2) Genentech Inc; WO 9426302 A 1994 HCAPLUS
- (3) Modi, P; WO 9636352 A 1996 HCAPLUS
- (4) Yamamoto, A; Journal of Controlled Release 1996, V41(1), P57

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844944	A2	19981015	WO 1998-US6825	19980407
WO 9844944	A3	19981230		
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ZA 9802950	A	19981019	ZA 1998-2950	19980407
AU 9869533	A1	19981030	AU 1998-69533	19980407
EP 973546	A2	20000126	EP 1998-915319	19980407
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
NO 9904879	A	19991207	NO 1999-4879	19991007
US 1997-42808		19970408		
GB 1997-9351		19970507		
WO 1998-US6825		19980407		
Human papillomavirus (HPV) antigen formulations are disclosed which prevent protein aggregation and show prolonged stability as aq. solns. These formulations comprise a salt (such as sodium chloride) and a non ionic surfactant (Polysorbate 80 such as Tween 80) in physiol. acceptable concns.				
9002-93-1, Triton x 100				
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(stabilized human papillomavirus antigen formulations that resist aggregation)				
9002-93-1 HCAPLUS				
Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)				





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L47 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:617622 HCAPLUS

DN 129:329667

TI Determination of the non-ionic detergent insolubility and phosphoprotein associations of glycosylphosphatidylinositol-anchored proteins expressed on T cells

AU Solomon, Keith R.; Mallory, Mark A.; Finberg, Robert W.

CS Infectious Disease Unit, Dana-Farber Cancer Institute, Boston, MA, 02115, USA

SO Biochem. J. (1998), 334(2), 325-333

CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.

DT Journal

LA English

AB Glycosylphosphatidylinositol (GPI)-anchored proteins are poorly solubilized in non-ionic detergents such as Triton X-100 and Nonidet P40, but are easily solubilized by detergents with high crit. **micelle** concns. such as octylglucoside. This soly. profile has been suggested to be due to the localization of GPI-anchored proteins to lipid microdomains rich in cholesterol and sphingolipids. Addnl., GPI-anchored proteins expressed on hemopoietic cells have been shown to assoc. with src-family tyrosine kinases and heterotrimeric G proteins. Despite these observations, the non-ionic detergent insoly. of GPI-anchored proteins on hemopoietic cells has not been quantified nor has a relation between the non-ionic detergent insoly. of these proteins and their assocn. with signal-transduction mols. been identified. Here the authors show that GPI-anchored proteins found on T-cell tumors and activated T cells, although significantly more insol. than transmembrane proteins, are not uniform in their detergent insoly. Whereas CD59 was between 4% and 13% sol., CD48 was between 13% and 25% sol., CD55 was between 20% and 30% sol., and CD109 was between 34% and 75% sol. The ability of these GPI-anchored proteins to assoc. with phosphoproteins was correlated with their detergent insoly.: the more detergent-insol. that a GPI-anchored protein was, the greater the level of phosphoprotein assocns. These expts. reveal a relation between non-ionic detergent insoly. and assocn. with signal-transduction mols. and suggest a cause-and-effect relation between these two properties. In total, these expts. support the hypothesis that the assocn. of GPI-anchored proteins with signaling mols. is due to their sorting to lipid microdomains.

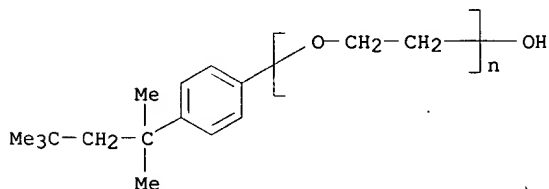
IT 9002-93-1, Triton X-100

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(T-cell GPI-anchored protein soly. in)

RN 9002-93-1 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 12

L47 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:71204 HCAPLUS

DN 128:145333

TI Preserving infectious recombinant **viruses** as aqueous suspensions  
in sucrose solutions for therapeutic use

IN Sene, Claude

PA Transgene S.A., Fr.; Sene, Claude

SO PCT Int. Appl., 27 pp.

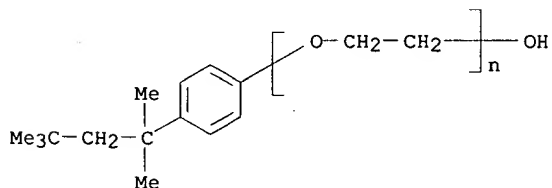
CODEN: PIXXD2

DT Patent

LA French

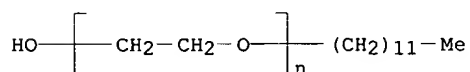
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9802522	A1	19980122	WO 1997-FR1308	19970715
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2751343	A1	19980123	FR 1996-8851	19960716
	FR 2751343	B1	19981218		
	CA 2232604	AA	19980122	CA 1997-2232604	19970715
	AU 9736986	A1	19980209	AU 1997-36986	19970715
	AU 711409	B2	19991014		
	EP 853660	A1	19980722	EP 1997-933740	19970715
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000500026	T2	20000111	JP 1998-505691	19970715
PRAI	FR 1996-8851		19960716		
	WO 1997-FR1308		19970715		
AB	A method for preserving infectious recombinant <b>viruses</b> , particularly adenovirus, in frozen or liq. form using a buffered aq. soln. contg. saccharose at 0.75-1.5 M (preferably 1M) and the therapeutic use of such a suspension are described. The use of sucrose as a stabilizer avoids the use of glycerol, which can be irritant to some mucous membranes, e.g. the lungs, and increase the storage lifetime of the <b>virus</b> at 4.degree. or -20.degree. to >6 mo without significant loss of titer. The medium is buffered and the <b>virus</b> is also stabilized with a monovalent and divalent cation. Nonionic detergents may also be added. Optimization expts. for stabilization of an adenovirus are reported. Conditions under which titers were retained with less than an order of magnitude loss (at .apprx.1010 pfu/mL) were obtained.				
IT	9002-93-1, Triton X-100				
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preserving infectious recombinant <b>viruses</b> as aq. suspensions in sucrose solns. for therapeutic use)				
RN	9002-93-1 HCAPLUS				
CN	Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)				



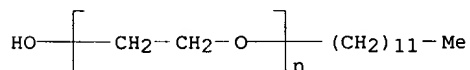
=&gt; d bib abs hitstr 13

L47 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1996:130069 HCAPLUS  
 DN 124:211827  
 TI Propellant-driven aerosols of proteins  
 AU Brown, Alan R.  
 CS Dep. of Diagnostic Medicine/Pathobiology, Kansas State Univ., Manhattan,  
 KS, 66506, USA  
 SO Aerosol Sci. Technol. (1996), 24(1), 45-56  
 CODEN: ASTYDQ; ISSN: 0278-6826  
 DT Journal  
 LA English  
 AB The protein bovine .gamma.-globulin was combined with surfactants,  
 suspended in a di-Me ether propellant, and delivered through metered-dose  
 aerosol valves to produce small particle aerosols of protein. A fraction  
 of the protein particles was of respirable size (.ltoreq.4 .mu.m  
 aerodynamic diam.) as detd. by cyclone or impactor aerosol sampling.  
 Protein/surfactant molar ratios of 1:1000 to 2000 produced the greatest  
 percentage of respirable-sized protein particles. Excessive surfactant  
 reduced the fraction of respirable-size particles, whereas too little  
 surfactant limited the suspension of protein in liquefied propellant. Low  
 protein/surfactant densities in propellant increased the fraction of  
 respirable-sized protein particles in aerosols, with 28-36% of aerosolized  
 protein of respirable size when protein concns. were 0.2 mg/mL of  
 propellant. Protein densities of up to 4 mg/mL in propellant could be  
 delivered as aerosols, but with a reduced respirable fraction. **Aq**  
**. solns.** of proteins at concns. of 1 to 2 mg/mL combined with  
 surfactants and then lyophilized to remove all water were aerosolized most  
 effectively when suspended in propellant. Addn. of glass beads or aerosol  
 vials enhanced the dispersion of agitated protein/surfactant suspensions  
 and improved protein aerosolization. Addn. of 2-4% ethanol in propellant  
 increased the fraction of respirable-size aerosol particles of protein  
 particles in aerosols. The potential of propellant-driven aerosols for  
 delivering therapeutic enzymes and antibodies, immuno-modulating  
 cytokines, and immunizing **vaccines** to the respiratory tract is  
 discussed.  
 IT 9002-92-0, Laureth-9  
 RL: THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)  
 (propellant-driven aerosols of proteins)  
 RN 9002-92-0 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA  
 INDEX NAME)



=&gt; d bib abs hitstr 14

L47 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1994:663544 HCAPLUS  
 DN 121:263544  
 TI Propellant-driven aerosols of functional proteins as potential therapeutic agents in the respiratory tract  
 AU Brown, Alan R.; Slusser, Joyce G.  
 CS Department of Pathology and Microbiology, College of Veterinary Medicine, Kansas State University, Manhattan, KS, 66506, USA  
 SO Immunopharmacology (1994), 28(3), 241-57  
 CODEN: IMMUDP; ISSN: 0162-3109  
 DT Journal  
 LA English  
 AB Aerosols of respirable-sized particles of functional proteins were delivered by volatile propellant from metered-dose aerosol canisters. The enzyme alk.-phosphatase and a monoclonal antibody were lyophilized with surfactant and suspended in the aerosol propellant dimethylether. As much as 20 .mu.g of functional protein, assessed by enzyme function or antibody binding activity, was delivered per 40 .mu.l of released propellant. Up to 25% of the protein was of respirable size (.ltoreq.4 .mu.m mass median aerodynamic diam.) when aerosolized proteins were sampled with a Casella cyclone. Respirable particles were derived from visible surfactant/protein complexes suspended in the liquefied propellant and from propellant-sol., nonsedimentable, surfactant/protein mols. that are probably reverse micelles. 10-14 days of propellant exposure in dimethylether increased protein soly. in the propellant, increased the total protein aerosolized and maintained or increased the quantity of respirable-sized protein mols., as compared to the day aerosol vials were charged with propellant. Scanning electron microscopic studies of the respirable-sized protein/surfactant particles showed that they ranged in size from 0.07 to 3.25 .mu.m in diam., and they appeared to be chain aggregates of spherical subunits, 0.11 to 0.93 .mu.m in diam. This structural motif was common to both proteins. The possibility of delivering immunizing antigens, cytokines, passive antibodies and other therapeutic proteins to the respiratory tract using propellant-driven aerosols is discussed.  
 IT 9002-92-0, Laureth 9  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (propellant-driven aerosols of functional proteins for respiratory tract)  
 RN 9002-92-0 HCAPLUS  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



572

CEPERLEY 09/647,518

=> d bib abs hitstr

L55 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS  
AN 1989:512018 HCAPLUS  
DN 111:112018  
TI Agglutination immunoassay and kit for determination of a multivalent  
immune species using a buffered salt wash solution  
IN Snyder, Brian Anthony; Belly, Robert Troconis  
PA Eastman Kodak Co., USA  
SO Eur. Pat. Appl., 9 pp.  
CODEN: EPXXDW  
DT Patent  
LA English  
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 280559	A2	19880831	EP 1988-301654	19880226
	EP 280559	A3	19900919		
	EP 280559	B1	19931020		
	R: CH, DE, FR, GB, LI, SE				
	US 4847199	A	19890711	US 1987-19850	19870227
	CA 1308349	A1	19921006	CA 1987-539760	19870616
	JP 63229366	A2	19880926	JP 1988-42396	19880226
PRAI	US 1987-19850		19870227		

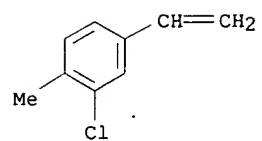
AB A test kit is used in an agglutination immunoassay to det. a multivalent immune species, such as Streptococcus A **antigen**, in a biol. sample. The method includes contacting an **aq. soln.** of the species with an agglutination indicator reagent having receptor mols. reactive with the species to form an agglutinate of the reaction product of species and receptor. These receptor mols. are bound to polymeric particles which contain tracer mols. The resulting agglutinate is captured on a microporous membrane which has an av. pore size which is .gtoreq.5 times greater than the av. diam. of the polymeric particles. Unagglutinated residual materials are washed through the membrane using a wash soln. which has a pH of 5-10 and an ionic strength .gtoreq.0.25. Tracer is then detd. either in the agglutinate or in the residual materials. The test kit includes the agglutination indicator reagent, the wash soln. and optionally an extn. compn. To prep. an agglutination reagent, Oil Red EGN was incorporated into core-shell polymer particles composed of a styrene-2-acetoacetoxyethyl methacrylate copolymer core, and an m,p-chloromethylstyrene homopolymer shell. Streptococcus A **antigen** monoclonal antibodies were covalently linked to the particles, which were then treated with succinic anhydride. The **antigen** was extd. from a clin. isolate with equal vols. of NaNO<sub>2</sub> (8 m) and citric acid (0.2M) and then neutralized with 3-(N-morpholino)propanesulfonic acid buffer (2M, pH 7.5) contg. EDTA (75 mM). A mixt. of NaCl (80 .mu.L, 1M), agglutination reagent (40 .mu.L) and extd. **antigen** (80 .mu.L, .apprx.4.2 .times. 10<sup>5</sup> CFU/mL) was added to the test well of a device contg. a nylon 66 membrane (5 .mu.m), incubated 2 min. at 25.degree., and allowed to drain through. Controls used distd. H<sub>2</sub>O and NaCl 0.025M as wash solns. The amt. of dye remaining on the membrane was measured at 540 nm by reflectance spectrophotometry. The 2 controls did not show adequate detention of the dye.

IT 122458-45-1D, monoclonal antibody conjugates  
RL: ANST (Analytical study)  
(Neisseria gonorrhoeae PIB **antigen** detn. by agglutination test using)

RN 122458-45-1 HCAPLUS  
CN 1,2-Ethanediol, monoacetate, polymer with 2-chloro-4-ethenyl-1-methylbenzene and ethenylbenzene (9CI) (CA INDEX NAME)

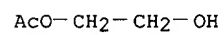
CM 1

CRN 105595-71-9  
CMF C9 H9 Cl



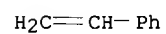
CM 2

CRN 542-59-6  
CMF C4 H8 O3



CM 3

CRN 100-42-5  
CMF C8 H8



CEPERLEY 09/647,518

=> d bib abs hitstr 1

L58 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:485461 HCAPLUS

DN 129:162000

TI Core/shell-type microspheres with good controllability of particle size and their preparation

IN Kataoka, Kazunori; Kato, Masao; Nagasaki, Sachio; Ijima, Michihiro; Fukuzawa, Sumiyo; Okano, Teruo

PA Kataoka, Kazunori, Japan

SO Jpn. Kokai Tokkyo Koho, 11 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 10195152	A2	19980728	JP 1996-356630	19961227
AB	Title microspheres, useful for carriers of drugs, are core/shell-type ones derived from stabilized polymer <b>micelles</b> obtained through polymn. of macromers shown as (HPLS-HPBS)-PLZA (HPLS = hydrophilic polymer segment; HPBS = hydrophobic polymer segment; PLZA = polymerizable group having ethylenically unsatd. double bonds linked to either terminal of HPLS or HPBS), whose core regions contain affinity polymers to core-forming polymer segments. Their prepn. is also claimed. Thus, a block copolymer (prepd. from 2-methoxyethanol 0.76, ethylene oxide 53, lactide 58, and methacrylic anhydride 23 g) was mixed with dimethylacetamide and V 65 (azobisisovaleronitrile), dialyzed against H2O, and polymd. to give stabilized polymer <b>micelles</b> , which was mixed with styrene and V 65 and polymd. to obtain core/shell-type microspheres with good controllability of particle size according to styrene addn. amt.				
IT	<b>210842-39-0P</b> RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (core-shell; prepn. of core/shell-type microspheres with good controllability of particle size)				
RN	210842-39-0 HCAPLUS				
CN	1,4-Dioxane-2,5-dione, 3,6-dimethyl-, polymer with ethenylbenzene and oxirane, 2-methoxyethyl ether, block, graft (9CI) (CA INDEX NAME)				

CM 1

CRN 109-86-4

CMF C3 H8 O2

HO-CH2-CH2-O-CH3

CM 2

CRN 210760-54-6

CMF (C8 H8 . C6 H8 O4 . C2 H4 O)x

CCI PMS

CDES 8:PM,BLOCK,GRAFT

CM 3

CRN 100-42-5

CMF C8 H8

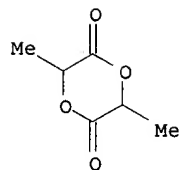
H2C=CH-Ph

CM 4

CRN 95-96-5

CEPERLEY 09/647,518

CMF C6 H8 O4  
CDES \*



CM 5

CRN 75-21-8  
CMF C2 H4 O





=&gt; d bib abs hitstr 2

L58 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:405695 HCAPLUS

DN 127:19957

TI Fabric conditioning compositions

IN Khoshdel, Ezat; Whaley, Christopher

PA Unilever Plc, UK

SO Brit. UK Pat. Appl., 30 pp.

CODEN: BAXXDU

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2304727	A1	19970326	GB 1995-18529	19950911

AB A fabric conditioning compn. comprises a fabric softening compd. such as quaternary ammonium compd. and a soil releasing copolymer polyether-polyester comprising (i) monomer units of poly(ethylene glycol) and/or capped poly(ethylene glycol); (ii) monomer units of an arom. dicarboxylic acid COArCOO (Ar = a bifunctional arom. group), (iii) monomer units, of a polyol having .gtoreq.3 OH groups CH2ACH2O (A = a bifunctional group contg. .gtoreq.1 C atom and .gtoreq.1 OH group). The polymer may be formed from polyethylene glycol, terephthalic acid and glycerol. A nonionic surfactant may be present as a stabilizer. A typical formulation included 0.005 g polyethylene glycol-glycerol-di-Me terephthalate copolymer (no.-av. mol. wt. 1700) added to 0.165 mL aq. soln. contg. 14.5% 1,2-bis(hydrogenated tallowoxyloxy)-3-trimethylammonium propane chloride/fatty acid 6:1.

IT 186910-35-0 186910-36-1  
 RL: MOA (Modifier or additive use); USES (Uses)  
 (soil release agents for fabric conditioning compns. for polyester or cotton fabric)

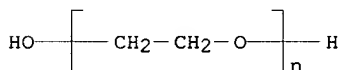
RN 186910-35-0 HCAPLUS  
 CN 1,4-Benzenedicarboxylic acid, dimethyl ester, polymer with .alpha.-hydro-.omega.-hydroxypoly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) and 1,2,3-propanetriol (9CI) (CA INDEX NAME)

CM 1

CRN 25322-68-3

CMF (C2 H4 O)n H2 O

CCI PMS

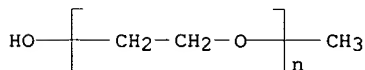


CM 2

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O

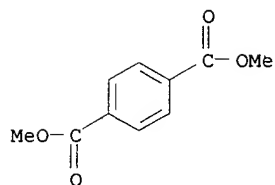
CCI PMS



CM 3

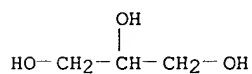
CRN 120-61-6

CMF C10 H10 O4



CM 4

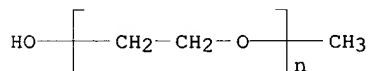
CRN 56-81-5  
CMF C3 H8 O3



RN 186910-36-1 HCAPLUS  
CN 1,4-Benzenedicarboxylic acid, dimethyl ester, polymer with  
.alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) and  
1,2,3-propanetriol (9CI) (CA INDEX NAME)

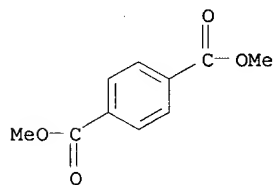
CM 1

CRN 9004-74-4  
CMF (C2 H4 O)n C H4 O  
CCI PMS



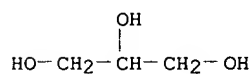
CM 2

CRN 120-61-6  
CMF C10 H10 O4



CM 3

CRN 56-81-5  
CMF C3 H8 O3



CEPERLEY 09/647,518

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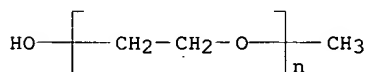
L58 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1996:731922 HCAPLUS  
 DN 126:31997  
 TI Poly(ethylene glycol) Graft Copolymers Containing Carboxylic Acid Groups: Aggregation and Viscometric Properties in **Aqueous Solution**  
 AU Derand, Helene; Wesslen, Bengt; Wittgren, Bengt; Wahlund, Karl-Gustav  
 CS Department of Chemical Engineering II, Lund University, Lund, S-221 00, Swed.  
 SO Macromolecules (1996), 29(27), 8770-8775  
 CODEN: MAMOBX; ISSN: 0024-9297  
 PB American Chemical Society  
 DT Journal  
 LA English  
 AB Poly(ethylene glycol) monomethyl ethers (MPEG) were grafted on copolymers of maleic anhydride and styrene, Me methacrylate, and ethylhexyl methacrylate, resp. Hydrolysis of the remaining anhydride residues gave graft copolymers carrying a large no. of carboxylic acid groups along the main chains. The properties in **aq. solns.** of these graft copolymers were studied with respect to aggregation behavior and viscometric properties. Aggregation of the polymers was examd. by quasi-elastic light scattering and flow field-flow fractionation in water and KCl soln. Both methods showed that the anionic graft copolymers mainly were present as single mols. in pure water, with a minor fraction of aggregates. In KCl soln., aggregates with av. sizes of approx. 30 nm were the dominant species. In **aq. soln.**, the polymers exhibited polyelectrolyte behavior, i.e., a dramatic increase of the viscosity upon neutralization. Graft copolymers with hydrophobic groups in the backbone had lower viscosities.

IT 53814-38-3  
 RL: PRP (Properties)  
 (aggregation and viscosity of aq. monomethyl poly(oxyethylene) graft copolymers contg. carboxylic acid groups)

RN 53814-38-3 HCAPLUS  
 CN 2,5-Furandione, polymer with ethenylbenzene, ester with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

CM 1

CRN 9004-74-4  
 CMF (C2 H4 O)<sub>n</sub> C H4 O  
 CCI PMS

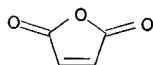


CM 2

CRN 9011-13-6  
 CMF (C8 H8 . C4 H2 O3)<sub>x</sub>  
 CCI PMS

CM 3

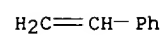
CRN 108-31-6  
 CMF C4 H2 O3



CEPERLEY 09/647,518

CM 4

CRN 100-42-5  
CMF C8 H8



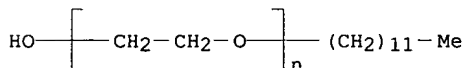
=&gt; d bib abs hitstr 4

L58 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2001 ACS  
 AN 1992:129953 HCAPLUS  
 DN 116:129953  
 TI Manufacture of water-soluble ester salts of itaconic acid copolymers  
 IN Wlasiuk, Danuta; Klopotek, Alojzy  
 PA Instytut Chemii Przemyslowej, Pol.  
 SO Pol., 11 pp. Abstracted and indexed from the unexamined application.  
 CODEN: POXXA7  
 DT Patent  
 LA Polish  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	PL 153127	B1	19910329	PL 1987-265244	19870417
AB	Products useful as complexing agents and surfactants are manufd. by partially esterifying 1-10:1-3 itaconic acid-maleic anhydride copolymers (I) with 0.01-2.5 mol C10-22 fatty alc., polyethoxylated C10-22 fatty alc. (d.p. 6-20), or polyethoxylated (C6-22-alkyl)phenol at 343-383 K and neutralizing with alkali metal hydroxides, NH3, and or alkanolamines at 293-323 K. Thus, a 130-600 I was heated in dioxane with 6 g polyethoxylated nonylphenol (d.p. 8) and stripped to give 245 g product (mol. wt. 5500) which was neutralized (240 g) with 763 g 20% NaOH at 293 K to give a 38.5% soln. of polymer with Ca2+ and Mg2+ complexation 82.9 and 0.9 mg/g at pH 9 and surface tension of a 0.5% aq. soln . 65 dynes/cm.				
IT	139247-10-2P				
RL:	PREP (Preparation)				
	(manuf. of water sol., for surfactants and complexing agents)				
RN	139247-10-2 HCAPLUS				
CN	Butanedioic acid, methylene-, polymer with 2,5-furandione, ester with .alpha.-dodecyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), potassium salt (9CI) (CA INDEX NAME)				

CM 1

CRN 9002-92-0  
 CMF (C2 H4 O)n C12 H26 O  
 CCI PMS

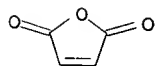


CM 2

CRN 28391-42-6  
 CMF (C5 H6 O4 . C4 H2 O3)x  
 CCI PMS

CM 3

CRN 108-31-6  
 CMF C4 H2 O3

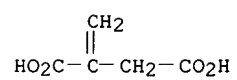


CM 4

CRN 97-65-4

CEPERLEY 09/647,518

CMF C5 H6 O4



=&gt; d bib abs hitstr 5

L58 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2001 ACS

AN 1992:42274 HCAPLUS

DN 116:42274

TI Preparation of melt-moldable and water-soluble thermoplastic modified maleic anhydride copolymer resins

IN Hirashima, Masao; Nozawa, Hiroshi; Kawame, Toshimitsu; Kono, Naotake

PA Kuraray Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 9 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03163109	A2	19910715	JP 1989-283638	19891030
	JP 2882648	B2	19990412		
PRAI	JP 1989-212407		19890817		

AB The title resins giving films with excellent phys. properties are prepd. by esterification of maleic anhydride copolymeres with RO(AO)nH I; R = C1-10 alkyl; A = (Ph-substituted) C2-4 vicinal alkylene; n .gtoreq.1]. Thus, after 30.8 g Isobam 04 (wt.-av. mol. wt. 5 .times. 104) was esterified with 17.8 g I (R = Me, A = CH2CH2, n = av. 6) (II) at 80-90.degree. for 5 h under N with stirring in 100 g DMF in the presence of 0.50 g 2-methylimidazole, the DMF and unreacted II were distd. off at 120.degree. under reduced pressure to obtain 39.5 g a partially esterified product (esterification degree 14.9%), which was pressed at 150.degree./50 kg/cm2(gage) for 3 min to prep. a 1-mm transparent film with softening temp. 120.degree. and breaking strength 80 kg/cm2 (gage) and breaking extension 30%. The obtained polyester 10, 25% aq. NH3 6.34, and H2O 50 g were stirred at 50-60.degree. for 30 min to give a transparent aq . soln..

IT 53814-38-3P 137462-36-3P 138414-49-0P  
138414-52-5P

RL: PREP (Preparation)

(prepn. of, thermoplastic and melt-moldable and water-sol, films with good phys. properties from)

RN 53814-38-3 HCAPLUS

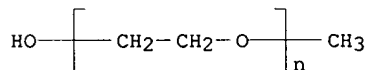
CN 2,5-Furandione, polymer with ethenylbenzene, ester with .alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl), graft (9CI) (CA INDEX NAME)

CM 1

CRN 9004-74-4

CMF (C2 H4 O)n C H4 O

CCI PMS



CM 2

CRN 9011-13-6

CMF (C8 H8 . C4 H2 O3)x

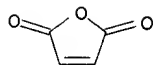
CCI PMS

CM 3

CRN 108-31-6

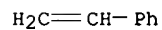
CMF C4 H2 O3





CM 4

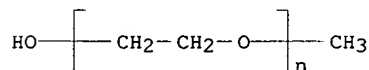
CRN 100-42-5  
CMF C8 H8



RN 137462-36-3 HCAPLUS  
CN 2,5-Furandione, polymer with 2-methyl-1-propene, ester with  
.alpha.-methyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX  
NAME)

CM 1

CRN 9004-74-4  
CMF (C2 H4 O)<sub>n</sub> C H4 O  
CCI PMS

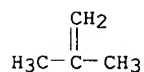


CM 2

CRN 26426-80-2  
CMF (C4 H8 . C4 H2 O3)<sub>x</sub>  
CCI PMS

CM 3

CRN 115-11-7  
CMF C4 H8



CM 4

CRN 108-31-6  
CMF C4 H2 O3

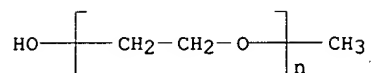


RN 138414-49-0 HCAPLUS  
CN 2,5-Furandione, polymer with ethene, ester with .alpha.-methyl-.omega.-  
hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

CM 1

CRN 9004-74-4

CMF (C2 H4 O)<sub>n</sub> C H4 O  
CCI PMS

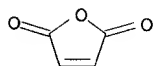


CM 2

CRN 9006-26-2  
CMF (C4 H2 O3 . C2 H4)<sub>x</sub>  
CCI PMS

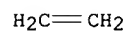
CM 3

CRN 108-31-6  
CMF C4 H2 O3



CM 4

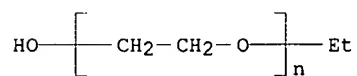
CRN 74-85-1  
CMF C2 H4



RN 138414-52-5 HCAPLUS  
CN 2,5-Furandione, polymer with 2-methyl-1-propene, ester with  
.alpha.-ethyl-.omega.-hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX  
NAME)

CM 1

CRN 27879-07-8  
CMF (C2 H4 O)<sub>n</sub> C2 H6 O  
CCI PMS



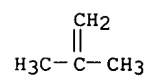
CM 2

CRN 26426-80-2  
CMF (C4 H8 . C4 H2 O3)<sub>x</sub>  
CCI PMS

CM 3

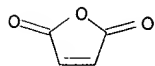
CRN 115-11-7  
CMF C4 H8

CEPERLEY 09/647,518



CM 4

CRN 108-31-6  
CMF C4 H2 O3



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=&gt; d ti pn 1-28

L74 ANSWER 1 OF 28 USPATFULL  
 TI Human papillomavirus vaccine formulations  
 PI US 6251678 B1 20010626

L74 ANSWER 2 OF 28 USPATFULL  
 TI Treatment of conditions and disease  
 PI US 6194392 B1 20010227

L74 ANSWER 3 OF 28 USPATFULL  
 TI Cascade polymer complexes, process for their production and  
 pharmaceutical agents containing said complexes  
 PI US 6177060 B1 20010123

L74 ANSWER 4 OF 28 USPATFULL  
 TI Cascade polymer complexes, process for their production and  
 pharmaceutical agents containing said complexes  
 PI US 6166200 20001226

L74 ANSWER 5 OF 28 USPATFULL  
 TI Use of hyaluronic acid or its derivatives to enhance delivery of  
 therapeutic agents  
 PI US 6069135 20000530  
 WO 9104058 19910404

L74 ANSWER 6 OF 28 USPATFULL  
 TI Cascade polymer complexes, process for their production and  
 pharmaceutical agents containing said complexes  
 PI US 6063361 20000516

L74 ANSWER 7 OF 28 USPATFULL  
 TI Treatment of conditions and disease  
 PI US 6048844 20000411

L74 ANSWER 8 OF 28 USPATFULL  
 TI Use of hyaluronic acid or its derivatives in peritoneal dialysis and  
 formulations thereof  
 PI US 5985851 19991116

L74 ANSWER 9 OF 28 USPATFULL  
 TI Compositions comprising hyaluronic acid and drugs  
 PI US 5985850 19991116

L74 ANSWER 10 OF 28 USPATFULL  
 TI Treatment of conditions and disease  
 PI US 5932560 19990803

L74 ANSWER 11 OF 28 USPATFULL  
 TI Treatment of conditions and disease  
 PI US 5929048 19990727

L74 ANSWER 12 OF 28 USPATFULL  
 TI Use of a form of hyaluronic acid and a medicinal agent for reducing  
 rejection of organs transplantation in mammals  
 PI US 5914314 19990622

L74 ANSWER 13 OF 28 USPATFULL  
 TI Treatment of conditions and disease  
 PI US 5852002 19981222

L74 ANSWER 14 OF 28 USPATFULL  
 TI Compositions containing a form of hyaluronic acid and a medicinal agent  
 for treating acne in mammals and methods for administration of such  
 composition  
 PI US 5830882 19981103

L74 ANSWER 15 OF 28 USPATFULL  
 TI Method of using hyaluronic acid or its pharmaceutically acceptable salts  
 for the treatment of disease

display not provided  
 for # 4, 6-8,  
 10-16, 23 & 25  
 since they are  
 related to a patent  
 all ready displayed  
 the kwic format  
 is provided when  
 the abstract is  
 lacking in hit terms

PI US 5827834 19981027

L74 ANSWER 16 OF 28 USPATFULL  
TI Cascade polymer complexes, process for their production and  
pharmaceutical agents containing said complexes  
PI US 5820849 19981013

L74 ANSWER 17 OF 28 USPATFULL  
TI Method of administering of a hyaluronic acid and an NSAID to decrease  
side effects of the NSAID  
PI US 5811410 19980922

L74 ANSWER 18 OF 28 USPATFULL  
TI **Vaccine** composition against influenza, with synergic effects,  
containing influenza **virus** core as an additive  
PI US 5741493 19980421

L74 ANSWER 19 OF 28 USPATFULL  
TI **Detergent**-facilitated immunoassay for the rapid and  
quantitative assay of pharmacological agents  
PI US 5627080 19970506

L74 ANSWER 20 OF 28 USPATFULL  
TI Contraceptive compositions  
PI US 5595980 19970121

L74 ANSWER 21 OF 28 USPATFULL  
TI Process for preparing immunogenic complexes and pharmaceutical  
composition containing these complexes  
PI US 4900549 19900213

L74 ANSWER 22 OF 28 USPATFULL  
TI Aryl and heteroaryl ethers as agents for the treatment of hypersensitive  
ailments  
PI US 4728668 19880301

L74 ANSWER 23 OF 28 USPATFULL  
TI Aryl and heteroaryl ethers as agents for the treatment of hypersensitive  
ailments  
PI US 4725619 19880216

L74 ANSWER 24 OF 28 USPATFULL  
TI Plasminogen activator derivatives  
PI US 4640835 19870203

L74 ANSWER 25 OF 28 USPATFULL  
TI Aryl and heteroaryl ethers as agents for the treatment of hypersensitive  
ailments  
PI US 4631287 19861223

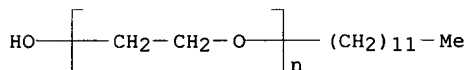
L74 ANSWER 26 OF 28 USPATFULL  
TI Composition for diagnostic reagents  
PI US 4578282 19860325

L74 ANSWER 27 OF 28 USPATFULL  
TI Preservative and fixative preparations for biological systems  
PI US 4493821 19850115

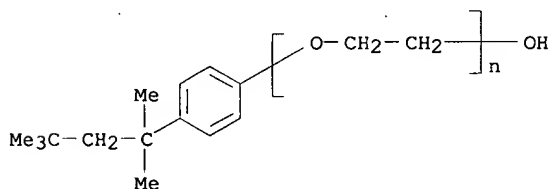
L74 ANSWER 28 OF 28 USPATFULL  
TI Process for the isolation of membrane proteins from Neisseria  
meningitidis and **vaccines** containing same  
PI US 4271147 19810602

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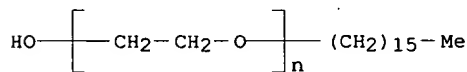
L74 ANSWER 1 OF 28 USPATFULL  
 AN 2001:97703 USPATFULL  
 TI Human papillomavirus **vaccine** formulations  
 IN Volkin, David B., Doylestown, PA, United States  
 Shi, Li, Eagleville, PA, United States  
 Mach, Henryk, Ambler, PA, United States  
 PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)  
 PI US 6251678 B1 20010626  
 AI US 2000-496812 20000202 (9)  
 PRAI US 1999-118723 19990205 (60)  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Salimi, Ali R.  
 LREP Giesser, Joanne M., Tribble, Jack L.  
 CLMN Number of Claims: 14  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
 LN.CNT 496  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB New human papilloma **virus** (HPV) **vaccine** formulations exhibit enhanced long-term stability. Formulation components can include: **virus**-like particles (VLPs) absorbed onto aluminum, a salt, non-ionic **surfactant**, and a buffer. Additional formulations also contain a polymeric polyanionic stabilizer and a salt either in the presence or absence buffering agents and nonionic **detergent**.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 9002-92-0, Brij35 9002-93-1, Triton x-100  
 9004-95-9, Brij 58  
 (surfactant; human papilloma virus vaccine formulations)  
 RN 9002-92-0 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9002-93-1 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9004-95-9 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-hexadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



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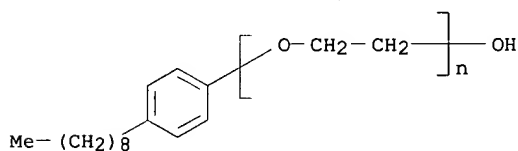
L74 ANSWER 2 OF 28 USPATFULL  
 AN 2001:29544 USPATFULL  
 TI Treatment of conditions and disease  
 IN Falk, Rudolf Edgar, Toronto, Canada  
 Asculai, Samuel S., Toronto, Canada  
 PA Hyal Pharmaceutical Corporation, Mississauga, Canada (non-U.S. corporation)  
 PI US 6194392 B1 20010227  
 AI US 1995-460978 19950807 (8)  
 RLI Division of Ser. No. US 1991-675908, filed on 3 Jul 1991  
 PRAI CA 1989-612307 19890921  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Peselev, Elli  
 LREP Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K.  
 CLMN Number of Claims: 16  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 2517

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A combination for administration to a mammal which combination employs a therapeutically effective amount of a medicinal and/or therapeutic agent to treat a disease or condition and an amount of hyaluronic acid and/or salts thereof and/or homologues, analogues, derivatives, complexes, esters, fragments and subunits of hyaluronic acid sufficient to facilitate the agent's penetration through the tissue (including scar tissue) at the site to be treated, through the cell membranes into the individual cells to be treated.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 26027-38-3, Nonoxynol-9  
 (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)  
 RN 26027-38-3 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



=&gt; d kwic 2

L74 ANSWER 2 OF 28 USPATFULL  
 SUMM . . . amount of solution given at each administration is generally less than 60 ml, e.g. less than 20 ml, of an **aqueous solution** of the acid or its salt. It is convenient to administer the acid dissolved in water (<2% w/w, buffered to. . .  
 SUMM . . . of an antiviral agent lacking inhibitory action and a compound (for example, hyaluronic acid) possessing cell fusion inhibitory activity and/or **virus**-adsorption inhibitory activity for treating disease carried by a **virus**.  
 SUMM . . . caused by retroviruses. Hyaluronic acid is taught for prevention or therapy of leukemia or AIDS by suppressing replication of the **virus**.  
 SUMM An article entitled "Inactivation of Herpes Simplex **Viruses** by Nonionic **Surfactants**" by one of the inventors herein (Dr. Samuel Asculai) among others (published in Antimicrobial Agents and Chemotherapy, April 1978, pp. . . . ether or amide linkages between



the hydrophilic and hydrophobic portions of the molecule rapidly inactivated the infectivity of herpes simplex **viruses**. The activity stemmed from the ability of nonionic **surfactants** to dissolve lipid-containing membranes. This was confirmed by observing **surfactant** destruction of mammalian cell plasma membranes and herpes simplex **virus** envelopes. Proprietary vaginal contraceptive formulations containing nonionic **surfactants** also inactivated herpes simplex **virus** infectivity. This observation suggests that nonionic **surfactants** in appropriate formulation could effectively prevent herpes simplex **virus** transmission."

- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . or condition (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic

**surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .

SUMM . . . . either intravenously, intra-arterially, intraperitoneally or intrapleurally or directly into the tumor by injection through a needle placed under sonographic or CT guidance.

SUMM According to another aspect of the invention, the combination of a non-ionic **surfactant** for example nonoxynol-9 [nonylphenoxy polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and hyaluronic acid and/or salts thereof and other. . . .

SUMM The non-ionic **surfactant** preferably comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule, being more active than the **surfactants** having an ester- or an ether- ester linkage.

SUMM The following nonionic **surfactants** and identified linkages are offered for consideration.

SUMM	Surfactant	Linkage
	None (control virus)	
	5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol)	Ether
	1% Triton X-100 (p-diisobutylphenoxy-polyethoxy Ether-ethanol)	Ether
	1% Brij-97 (polyoxyethylene (10) oleyl ether)	Ether
	1% Span-20 (sorbitran monclamate)	Ester
	1% Span-80. . . .	
SUMM	(h) non-antigenic."	
SUMM	. . . . person suffering brain trauma	
2.	Hair growth	minoxidil - combination - grow more hair when applied topically
3.	Herpes, canker sore, shingles	nonionic <b>surfactants</b> , e.g., nonoxynol-9 and anionic, (e.g. cetyl pyridinium chloride) and cationic (e.g. benzalkonium choride), <b>surfactants</b>
4.	Renal failure, cardiac insufficiency, hypertension, edema	diuretics - furosemide
5.	Infection, acne, mononucleosis	antibiotics, antibacterials, antimicrobials, etc., ascorbic acid and hyaluronic. . . .
DETD	On sequential CT scan this patient shows significant improvement in size of the residual mass. As soft tissue sarcomas are so very resistant. . . .	
DETD	Patient was given CT Scan of the abdomen and pelvis. There is moderate hepatic steatosis without evidence of metastatic disease. The spleen, pancreas, adrenals. . . .	
DETD	. . . . treatment, the patient has made good improvement. She has gained weight, and is no longer feeling any pain. The carcinoembryonic antigen is down to 26 nonograms/ml and steadily falling.	
DETD	. . . . and an MRI scan was undertaken to try and demonstrate this. It showed somewhat abnormalities in the appropriate area. A CT scan of the region was unhelpful.	
DETD	This man has a mesothelioma following surgical resection and then adjuvant treatment. It is now seven years since the initial diagnosis. In the spring of this year he developed a recurrence. . . .	
DETD	. . . . biopsy, but apparently there was regrowth and worsening of the pain with partial ureteric obstruction demonstrated as shown by a CT scan of the abdomen and pelvis done Jun. 28, 1990.	
IT	26027-38-3, Nonoxynol-9 (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)	

=&gt; d bib abs hitstr 3

L74 ANSWER 3 OF 28 USPATFULL  
 AN 2001:10522 USPATFULL  
 TI Cascade polymer complexes, process for their production and pharmaceutical agents containing said complexes  
 IN Schmitt-Willich, Heribert, Berlin, Germany, Federal Republic of  
 Platzek, Johannes, Berlin, Germany, Federal Republic of  
 Raduchel, Bernd, Berlin, Germany, Federal Republic of  
 Muhler, Andreas, Neuenhagen, Germany, Federal Republic of  
 Frenzel, Thomas, Berlin, Germany, Federal Republic of  
 PA Schering Aktiengesellschaft, Berlin, Germany, Federal Republic of (non-U.S. corporation)  
 PI US 6177060 B1 20010123  
 AI US 1998-44254 19980319 (9)  
 RLI Division of Ser. No. US 1996-674844, filed on 3 Jul 1996, now patented, Pat. No. US 5820849  
 PRAI DE 1995-19525924 19950704  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Hartley, Michael G.  
 LREP Millen, White, Zelano & Branigan, P.C.  
 CLMN Number of Claims: 8  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 1880  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Cascade polymer complexes with at least 16 ions of an element of atomic numbers 20 to 29, 39, 42, 44 or 57-83, useful NMR or x-ray lymphography imaging.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 23601-40-3, Hexaethylene glycol monomethyl ether  
 (prepn. of cascade polymer complexes as medical contrast media)  
 RN 23601-40-3 USPATFULL  
 CN 2,5,8,11,14,17-Hexaoxanonadecan-19-ol (8CI, 9CI) (CA INDEX NAME)

PAGE 1-A

$$\text{MeO}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}_2-\text{O}-$$

PAGE 1-B

$$-\text{CH}_2-\text{CH}_2-\text{OH}$$

(1) an agent selected from a medicinal agent and a therapeutic agent and combinations thereof in a therapeutically effective amount to treat a disease or condition in humans who will benefit from the treatment with the agent; and

(2) hyaluronic acid and/or pharmaceutically acceptable salts thereof and/or fragments, and subunits of hyaluronic acid, characterized in that said composition

(a) is in a dosage form which is suitable for administration in humans;  
and

(b) is in a form in which (i) component (1) is in an effective dosage amount to treat said disease or condition by penetration at the site to be treated; and (ii) component (2) is immediately available to transport component (1) at the site to be treated, and which component (2) is in an effective non-toxic amount to facilitate the transport of component (1) upon administration, through the tissue including scar tissue, at the site to be treated and through the cell membranes or the individual cells to be treated, wherein said amount of component (2) is sufficient to provide a dosage greater than 10 mg/70 kg person of component (2).

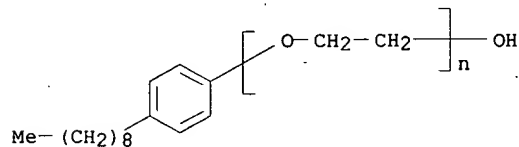
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 26027-38-3, Nonoxynol-9

(hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)

RN 26027-38-3 USPATFULL

CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
(CA INDEX NAME)



=&gt; d kwic 5

## L74 ANSWER 5 OF 28 USPATFULL

SUMM . . . amount of solution given at each administration is generally less than 60 ml, e.g. less than 20 ml, of an **aqueous solution** of the acid or its salt. It is convenient to administer the acid dissolved in water (<2% w/w, buffered to. . .

SUMM . . . of an antiviral agent lacking inhibitory action and a compound [for example, hyaluronic acid] possessing cell fusion inhibitory activity and/or **virus-adsorption** inhibitory activity for treating disease carried by a **virus**.

SUMM . . . action, being perhaps anesthetics, analgesics, anti inflammatories, wound healers, antimicrobics, adrenergic agonists and antagonists, cytostatics, antirheumatics, antihypertensives, diuretics, sexual hormones, **immunostimulants** and immunosuppressants, for example, one of the drugs having the activity already described for the therapeutically active alcohols to be. . .

SUMM . . . caused by retroviruses. Hyaluronic acid is taught for prevention or therapy of leukemia or AIDS by suppressing replication of the **virus**.

SUMM An article entitled "Inactivation of Herpes Simplex **Viruses** by Nonionic **Surfactants**" by one of the inventors herein (Dr. Samuel Asculai) among others [published in Antimicrobial Agents and Chemotherapy, April 1978, pp.686-690]. . . ether or amide linkages between the hydrophilic and hydrophobic portions of the molecule rapidly inactivated the infectivity of herpes simplex **viruses**. The activity stemmed from the ability of nonionic **surfactants** to dissolve lipid-containing membranes. This was confirmed by observing **surfactant** destruction of mammalian cell plasma membranes and herpes simplex **virus** envelopes. Proprietary vaginal contraceptive formulations containing nonionic **surfactants** also inactivated herpes simplex **virus** infectivity. This observation suggests that nonionic **surfactants** in appropriate formulation could effectively prevent herpes simplex **virus** transmission."

DETD . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the. . .

DETD . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the. . .

DETD . . . radical scavenger (for example ascorbic acid (Vitamin C)), vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the. . .

DETD . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal

- anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the . . . .
- DETD . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the . . . .
- DETD . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the . . . .
- DETD . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-viral agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (.+-. ) tromethamine salt of ketorolac (sold under the . . . .
- DETD . . . . either intravenously, intra-arterially, intraperitoneally or intrapleurally or directly into the tumor by injection through a needle placed under sonographic or CT guidance.
- DETD According to another aspect of the invention, the combination of a non-ionic **surfactant** for example nonoxynol-9 [nonylphenoxy polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and hyaluronic acid and/or salts thereof and other. . . .
- DETD The non-ionic **surfactant** preferably comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the molecule, being more active than the **surfactants** having an ester--or an ether--ester linkage.
- DETD The following nonionic **surfactants** and identified linkages are offered for consideration.
- DETD

Surfactant	Linkage
None (control virus)	
5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol)	Ether
1% Triton X-100 (p-diisobutylphenoxy-polyethoxy ethanol)	Ether
1% Brij-97 (polyoxyethylene (10) oleyl ether)	Ether
1% Span-20 (sorbitran monclamate)	Ester
1% Span-80 (sorbitan. . . .	
DETD (h) non-antigenic."	
DETD . . . . person suffering brain trauma	
2. Hair growth	minoxidil - combination - grow more hair when applied topically
3. Herpes, canker sore, shingles	nonionic <b>surfactants</b> , e.g., nonoxynol-9 and anionic, (e.g. cetyl pyridinium chloride) and cationic (e.g. benzalkonium choride), <b>surfactants</b>
4. Renal failure, cardiac	

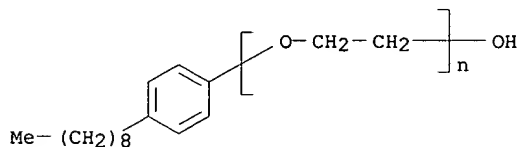
- diuretics - furosemide  
insufficiency, hypertension,  
edema
5. Infection, acne, antibiotics, antibacterials,  
mononucleosis antimicrobials, etc.,  
ascorbic  
acid and hyaluronic. . . .
- DETD On sequential CT scan this patient shows significant  
improvement in size of the residual mass. As soft tissue sarcomas are so  
very resistant. . . .
- DETD Patient was given CT Scan of the abdomen and pelvis. There is  
moderate hepatic steatosis without evidence of metastatic disease. The  
spleen, pancreas, adrenals. . . .
- DETD . . . . treatment, the patient has made good improvement. She has  
gained weight, and is no longer feeling any pain. The carcinoembryonic  
**antigen** is down to 26 nonograms/ml and steadily falling.
- DETD . . . . and an MRI scan was undertaken to try and demonstrate this. It  
showed somewhat abnormalities in the appropriate area. A CT  
scan of the region was unhelpful.
- DETD This man has a mesothelioma following surgical resection and then  
**adjuvant** treatment. It is now seven years since the initial  
diagnosis. In the spring of this year he developed a recurrence. . . .
- DETD . . . . biopsy, but apparently there was regrowth and worsening of the  
pain with partial ureteric obstruction demonstrated as shown by a  
CT scan of the abdomen and pelvis done Jun. 28, 1990.
- CLM What is claimed is:  
. . . the agent is selected from the group consisting of free radical  
scavengers, ascorbic acid (Vitamin C), anti-cancer drugs,  
chemotherapeutic drugs, anti-viral drugs, non-steroidal  
anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs,  
anti-fungal drugs, detoxifying drugs, analgesics, bronchodilators,  
anti-bacterial drugs, antibiotic drugs for treatment. . . .  
6. The method of claim 1 or 2 wherein the agent is an anti-viral  
drug.
21. The method of claim 1 or 2 wherein the agent is a non-ionic  
**surfactant** drug.
26. The method of claim 21 wherein the non-ionic **surfactant** is  
nonoxynol-9.
27. The method of claim 21 wherein the non-ionic **surfactant**  
further comprises an ether or an amide linkage between the hydrophilic  
and hydrophobic portions of the **surfactant**.
32. The method of claim 1 or 2 wherein the disease or condition is  
selected from the group consisting of a neoplastic condition, acne,  
AIDS, Berger's disease, a condition requiring bronchodilation, canker  
sore, chronic bacterial infection, fungal infection, diabetes,  
**viral** disease, epitheloid sarcoma, herpes, shingles,  
hypertension, infection, inflammation, malfunctioning kidney, renal  
failure, kyphosis, leomyosarcoma, leukemia, mesothelioma, metastatic  
disease, mononucleosis, pain, . . . .  
. . . of claim 1 or 2 wherein the disease or condition is a canker sore and  
wherein the agent is a **surfactant** selected from the group  
consisting of non-ionic **surfactants**, ionic **surfactants**  
and cationic **surfactants**.
41. The method of claim 40 wherein the **surfactant** is selected  
from the group consisting of nonoxynol-9, cetyl pyridinium chloride and  
benzalkonium chloride.
45. The method of claim 1 or 2 wherein the disease or condition is  
**viral** disease.
- . . . The method of claim 1 or 2 wherein the disease or condition is herpes  
and wherein the agent is a **surfactant** selected from the group  
consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium  
chloride.

- . . . The method of claim 1 or 2 wherein the disease or condition is shingles and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
  - . . . the agent is selected from the group consisting of free radical scavengers, ascorbic acid (Vitamin C), anti-cancer drugs, chemotherapeutic drugs, anti-viral drugs, non-steroidal anti-inflammatory drugs (NSAID), steroidal anti-inflammatory drugs, anti-fungal drugs, detoxifying drugs, analgesics, bronchodilators, anti-bacterial drugs, antibiotic drugs for treatment. . .
  - 71. The method of claim 66 or 67 wherein the agent is an anti-viral drug.
  - 86. The method of claim 66 or 67 wherein the agent is a non-ionic **surfactant** drug.
  - 91. The method of claim 86 wherein the non-ionic **surfactant** is nonoxynol-9.
  - 92. The method of claim 86 wherein the non-ionic **surfactant** further comprises an ether or an amide linkage between the hydrophilic and hydrophobic portions of the **surfactant**.
  - 97. The method of claim 66 or 67 wherein the disease or condition is selected from the group consisting of a neoplastic condition, acne, AIDS, Berger's disease, a condition requiring bronchodilation, canker sore, chronic bacterial infection, fungal infection, diabetes, viral disease, epitheloid sarcoma, herpes, shingles, hypertension, infection, inflammation, malfunctioning kidney, renal failure, kyphosis, leiomyosarcoma, leukemia, mesothelioma, metastatic disease, mononucleosis, pain, . . .
  - . . . of claim 66 or 67 wherein the disease or condition is a canker sore and wherein the agent is a **surfactant** selected from the group consisting of non-ionic **surfactants**, ionic **surfactants** and cationic **surfactants**.
  - 106. The method of claim 105 wherein the **surfactant** is selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
  - 110. The method of claim 66 or 67 wherein the disease or condition is viral disease.
  - . . . The method of claim 66 or 67 wherein the disease or condition is herpes and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
  - . . . The method of claim 66 or 67 wherein the disease or condition is shingles and wherein the agent is a **surfactant** selected from the group consisting of nonoxynol-9, cetyl pyridinium chloride and benzalkonium chloride.
- IT 26027-38-3, Nonoxynol-9  
(hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)



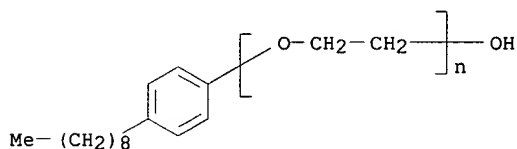
=> d bib abs hitstr 9

L74 ANSWER 9 OF 28 USPATFULL  
 AN 1999:146549 USPATFULL  
 TI Compositions comprising hyaluronic acid and drugs  
 IN Falk, Rudolf Edgar, Toronto, Canada  
 Asculai, Samuel S., Toronto, Canada  
 PA Hyal Pharmaceuticals Corporation, Mississauga, Canada (non-U.S.  
 corporation)  
 PI US 5985850 19991116  
 AI US 1995-462154 19950605 (8)  
 RLI Division of Ser. No. US 675908  
 PRAI CA 1989-612307 19890921  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Peselev, Elli  
 LREP Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K.  
 CLMN Number of Claims: 92  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 2760  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB A dosage amount of a pharmaceutical composition comprising a  
 therapeutically effective amount of an agent to treat a disease or  
 condition involving underperfused tissue and pathological tissue in  
 humans and a form of hyaluronic acid, wherein the form of hyaluronic  
 acid is available to transport the agent from the point of  
 administration to the site to be treated.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 26027-38-3, Nonoxynol-9  
 (hyaluronate or salt or deriv. and, for treating herpes, canker sores  
 and shingles, penetration enhancement in relation to)  
 RN 26027-38-3 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



=&gt; d bib abs hitstr 17

L74 ANSWER 17 OF 28 USPATFULL  
 AN 1998:115725 USPATFULL  
 TI Method of administering of a hyaluronic acid and an NSAID to decrease side effects of the NSAID  
 IN Falk, Rudolf Edgar, Toronto, Canada  
 Asculai, Samuel S., Toronto, Canada  
 PA Hyal Pharmaceutical Corporation, Mississauga, Canada (non-U.S. corporation)  
 PI US 5811410 19980922  
 AI US 4653351 19950605 (8)  
 RLI Division of Ser. No. 675908, filed on 3 Jul 1991  
 PRAI CA 612307 19890921  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Fonda, Kathleen K.  
 LREP Hughes, Ivor M., Hughes, Neil H., Sarkis, Marcelo K.  
 CLMN Number of Claims: 7  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 2340  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB A method of administering a medicinal agent and an effective amount of a form of hyaluronic acid for decreasing side effects associated with using the agent alone in treating a disease or condition in mammals is disclosed. The agent may be a non-steroidal anti-inflammatory drug (NSAID). The amount of hyaluronic acid is sufficient enough to provide a dosage greater than 200 mg/70 kg person. The molecular weight of the form of hyaluronic acid may be less than 750,000 daltons.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 26027-38-3, Nonoxynol-9  
 (hyaluronate or salt or deriv. and, for treating herpes, canker sores and shingles, penetration enhancement in relation to)  
 RN 26027-38-3 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



=&gt; d kwic 17

L74 ANSWER 17 OF 28 USPATFULL  
 SUMM . . . amount of solution given at each administration is generally less than 60 ml, e.g. less than 20 ml, of an **aqueous solution** of the acid or its salt. It is convenient to administer the acid dissolved in water (<2% w/w, buffered to. . .  
 SUMM . . . of an antiviral agent lacking inhibitory action and a compound [for example, hyaluronic acid] possessing cell fusion inhibitory activity and/or **virus**-adsorption inhibitory activity for treating disease carried by a **virus**.  
 SUMM . . . action, being perhaps anesthetics, analgesics, anti inflammatories, wound healers, antimicrobics, adrenergic agonists and antagonists, cytostatics, antirheumatics, antihypertensives, diuretics, sexual hormones, **immunostimulants** and immunosuppressants, for example, one of the drugs having the activity already described for the therapeutically active alcohols to be. . .  
 SUMM . . . caused by retroviruses. Hyaluronic acid is taught for

- prevention or therapy of leukemia or AIDS by suppressing replication of the **virus**.
- SUMM An article entitled "Inactivation of Herpes Simplex **Viruses** by Nonionic **Surfactants**" by one of the inventors herein (Dr. Samuel Asculai) among others [published in Antimicrobial Agents and Chemotherapy, April 1978, pp.686-690]. . . . ether or amide linkages between the hydrophilic and hydrophobic portions of the molecule rapidly inactivated the infectivity of herpes simplex **viruses**. The activity stemmed from the ability of nonionic **surfactants** to dissolve lipid-containing membranes. This was confirmed by observing **surfactant** destruction of mammalian cell plasma membranes and herpes simplex **virus** envelopes. Proprietary vaginal contraceptive formulations containing nonionic **surfactants** also inactivated herpes simplex **virus** infectivity. This observation suggests that nonionic **surfactants** in appropriate formulation could effectively prevent herpes simplex **virus** transmission."
- SUMM . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-**viral** agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-**viral** agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-**viral** agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-**viral** agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .
- SUMM . . . . radical scavenger (for example ascorbic acid (Vitamin C)), Vitamin C (for the treatment of mononucleosis), an anti-cancer agent, chemotherapeutic agent, anti-**viral** agents for example a nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy ethanol] found in Delfen.TM. contraceptive cream, and anionic **surfactants** (e.g. cetyl pyridinium chloride) and cationic **surfactants** (e.g. benzalkonium chloride), non-steroidal anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and (+/-) tromethamine salt of ketorolac (sold under the. . . .

SUMM (+/-) tromethamine salt of ketorolac (sold under the. . . .  
 . . . . radical scavenger (for example ascorbic acid (Vitamin C)),  
 Vitamin C (for the treatment of mononucleosis), an anti-cancer agent,  
 chemotherapeutic agent, anti-viral agents for example a  
 nonionic **surfactant**, e.g. nonoxynol-9 [nonylphenoxy polyethoxy  
 ethanol] found in Delfen.TM. contraceptive cream, and anionic  
**surfactants** (e.g. cetyl pyridinium chloride) and cationic  
**surfactants** (e.g. benzalkonium chloride), non-steroidal  
 anti-inflammatory drugs (NSAID) for example indomethacin, naproxen and  
 (+/-) tromethamine salt of ketorolac (sold under the. . . .  
 SUMM . . . . either intravenously, intra-arterially, intraperitoneally or  
 intrapleurally or directly into the tumor by injection through a needle  
 placed under sonographic or CT guidance.  
 SUMM According to another aspect of the invention, the combination of a  
 non-ionic **surfactant** for example nonoxynol-9 [nonylphenoxy  
 polyethoxy ethanol] [found in Delfen (t.m.) contraceptive cream] and  
 hyaluronic acid and/or salts thereof and other. . . .  
 SUMM The non-ionic **surfactant** preferably comprises an ether or an  
 amide linkage between the hydrophilic and hydrophobic portions of the  
 molecule, being more active than the **surfactants** having an  
 ester- or an ether-ester linkage.  
 SUMM The following nonionic **surfactants** and identified linkages are  
 offered for consideration.

SUMM

Surfactant	Linkage
------------	---------

None (control virus)

5% Nonoxynol-9 (nonylphenoxy-polyethoxy ethanol)

Ether

1% Triton X-100 (p-diisobutylphenoxy-polyethoxy-

Ether

ethanol)

1% Brij-97 (polyoxyethylene (10) oleyl ether)

Ether

1% Span-20 (sorbitran monclamate)

Ester

1% Span-80 (sorbitan. . . .

SUMM (h) non-antigenic."

SUMM . . . . person suffering brain trauma

2. Hair growth minoxidil - combination -  
 grow more hair when applied  
 topically

3. Herpes, canker sore,

shingles nonionic **surfactants**, e.g.,  
 nonoxynol-9 and  
 anionic, (e.g. cetyl  
 pyridinium chloride) and  
 cationic (e.g.  
 benzalkonium choride),  
**surfactants**

4. Renal failure, cardiac

diuretics - furosemide  
 insufficiency, hypertension,  
 edema

5. Infection, acne, antibiotics, antibacterials,  
 mononucleosis antimicrobials, etc.,  
 ascorbic  
 acid and hyaluronic. . . .

DETD On sequential CT scan this patient shows significant  
 improvement in size of the residual mass. As soft tissue sarcomas are so  
 very resistant. . . .

DETD Patient was given CT Scan of the abdomen and pelvis. There is  
 moderate hepatic steatosis without evidence of metastatic disease. The  
 spleen, pancreas, adrenals. . . .

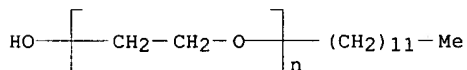
DETD . . . . treatment, the patient has made good improvement. She has  
 gained weight, and is no longer feeling any pain. The carcinoembryonic  
**antigen** is down to 26 nonograms/ml and steadily falling.

DETD . . . . and an MRI scan was undertaken to try and demonstrate this. It  
 showed somewhat abnormalities in the appropriate area. A CT  
 scan of the region was unhelpful.

DETD This man has a mesothelioma following surgical resection and then  
adjuvant treatment. It is now seven years since the initial  
diagnosis. In the spring of this year he developed a recurrence. . . .  
DETD . . . biopsy, but apparently there was regrowth and worsening of the  
pain with partial ureteric obstruction demonstrated as shown by a  
CT scan of the abdomen and pelvis done Jun. 28, 1990.  
IT 26027-38-3, Nonoxynol-9  
(hyaluronate or salt or deriv. and, for treating herpes, canker sores  
and shingles, penetration enhancement in relation to)

=&gt; d bib abs hitstr 18

L74 ANSWER 18 OF 28 USPATFULL  
 AN 1998:42069 USPATFULL  
 TI **Vaccine** composition against influenza, with synergic effects, containing influenza **virus** core as an additive  
 IN Moste-Deshairs, Catherine, Ecully, France  
 Meignier, Bernard, Thurins, France  
 PA Pasteur Merieux Serums et Vaccins, Lyons, France (non-U.S. corporation)  
 PI US 5741493 19980421  
 AI US 1995-375224 19950119 (8)  
 RLI Continuation of Ser. No. US 1992-927261, filed on 22 Nov 1992, now abandoned  
 PRAI FR 1991-806 19910124  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Minnifield, N. M.  
 LREP Curtis Morris & Safford P.C.  
 CLMN Number of Claims: 56  
 ECL Exemplary Claim: 1  
 DRWN 7 Drawing Figure(s); 2 Drawing Page(s)  
 LN.CNT 946  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB The use, when preparing a **vaccine** composition containing a standard influenza **virus vaccine**, of an additive which consists of a core or core fraction of at least one influenza **virus**, especially a fraction containing protein M; and a **vaccine** composition thereby obtained. The use of said additive improves the **vaccine's** effectiveness.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 9002-92-0  
 (in M protein sepn. for influenza vaccine component)  
 RN 9002-92-0 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d kwic 18

L74 ANSWER 18 OF 28 USPATFULL  
 TI **Vaccine** composition against influenza, with synergic effects, containing influenza **virus** core as an additive  
 AB The use, when preparing a **vaccine** composition containing a standard influenza **virus vaccine**, of an additive which consists of a core or core fraction of at least one influenza **virus**, especially a fraction containing protein M; and a **vaccine** composition thereby obtained. The use of said additive improves the **vaccine's** effectiveness.  
 SUMM The object of the present invention is a **vaccine** composition against influenza, with synergic effects, containing influenza **virus** core, or a fraction thereof, as an additive to the influenza **vaccine**.  
 SUMM The influenza **virus** comprises a lipoprotein envelope surrounding a nucleoprotein "core". The envelope more particularly includes two glycoproteins, hemagglutinin (HA) and neuraminidase (NA). The core is a complex arrangement of viral ribonucleic acid and of several so-called "internal" proteins (polymerases, membrane protein (M) and nucleoprotein (NP)).  
 SUMM At present it is known that the influenza **vaccine**, even when correctly applied, does not completely protect all the subjects **vaccinated**: see for example Murphy & Webster, in 'Virology, 2ns

edition (Fields et al. Ed.) 1091-1152 (1990), in particular p. 1128.

SUMM It was therefore desirable to improve the existing **vaccines**.

SUMM The influenza **vaccines** currently used are inactivated **vaccines**: they may be constituted of entire virions, or of virions subjected to treatment with agents which dissolve lipids ("split" **vaccines**), or else of purified glycoproteins ("sub-unit **vaccines**"). These inactivated **vaccines** mainly protect by causing synthesis of the receiver's antibodies directed against the hemagglutinin. It is known that **antigenic** evolution of the influenza **virus** by mutation results basically in modifications in HA and NA, while the internal proteins are only slightly modified. The result is that inactivated **vaccines** used at present only protect effectively as regards the strains the surface glycoproteins of which are identical or **antigenically** very close to those of the **vaccine** strains. To obtain a sufficient **antigenic** spectrum, the **vaccines** are obtained from several **viral** strains; they generally contain two type A strains and one type B strain. To adapt the composition of the **vaccines** to the **antigenic** evolution of the influenza **viruses**, the choice of strains for use in the **vaccines** is reviewed annually depending on the WHO or the American Food and Drug Administration recommendations, these recommendations being based on the results of international epidemiological observations. It is known that the recommended **viral** strains may be obtained notably from the the following organisations:

SUMM It has now been discovered that it is possible to obtain a **vaccine** composition with synergic effect by associating influenza **virus** core, or an active fraction of core, with the conventional influenza **vaccine**.

SUMM An active core fraction is one which, when used as an additive to a conventional **vaccine**, improves the effect of the **vaccine**.

SUMM Moreover, a protection against **virus** subtypes not used in the preparation of the components of the **vaccine** (conventional and added core or core fraction) may be obtained.

SUMM The object of the present invention, then, is a **vaccine** composition against influenza containing the constituents of a conventional influenza **vaccine**, and further containing core of at least one influenza **virus** strain, or a fraction of the said core, as an additive.

SUMM The conventional **vaccine** forming the main constituent of the **vaccine** composition of the invention may be an anti-influenza **vaccine** with complete virions, a sub-unit **vaccine** or a split **vaccine**. It may be obtained from **viruses** cultivated in chick embryonated eggs, or on cells.

SUMM The conventional **vaccines** may be prepared according to known methods, which are described by Murphy & Wzbster, op. cit., for example. Other details. . . .

SUMM Complete Virion **Vaccine**: this may be prepared as follows: the influenza **virus**, obtained by culture on chick embryonated eggs, or by culture on cells, is concentrated by ultrafiltration and then purified by. . . .

SUMM Subunit **Vaccine**: such a **vaccine** may be prepared as follows: using **viral** suspensions fragmented by treatment with **detergent**, the surface **antigens** (hemagglutinin, neuraminidase) are purified, by ultracentrifugation for example. The sub-unit **vaccines** thus contain mainly HA protein, and possible NA.

SUMM The **detergent** used by be cationic **detergent** for example, such as hexadecyl trimethyl ammonium bromide (Bachmeyer, Intervirology, 5, 260-272 (1975)), an anionic **detergent** such as ammonium deoxycholate (Laver & Webster, Virology 69, 511-522, 1976; Webster et al., The Journal of Immunology, Vol. 119, 2073-2077, 1977); or a nonionic **detergent** such as that commercialized under the name TRITON X100.

SUMM Split **Vaccine**: It can be prepared as follows: an aqueous suspension of the purified **virus** obtained as above, inactivated or not, is treated, under stirring, by lipid solvents such as ethyl ether or chloroform, associated with **detergents**. The

dissolution of the **viral** envelope lipids results in fragmentation of the **viral** particles. The aqueous phase is recuperated containing the split **vaccine**, constituted mainly of hemagglutinin and neuraminidase with their original lipid environment removed, and the core or its degradation products. Then. . .

SUMM Conventional **vaccines** generally contain 10 to 15 .mu.g of hemagglutinin from each of the strains entering into their composition.

SUMM The conventional influenza **vaccine** forming the main constituent of the **vaccine** composition of the invention may originate from a **virus** of type A, B or C, or from at least two of these three types. The same applies to the. . .

SUMM The core or fraction of core may be prepared from **viruses** from the same strain as the main constituent of the composition, or from a different strain or strains, which may. . .

SUMM The nomenclature of the influenza **viruses** and their classification into types and sub-types are described for example in WHO Bull. 58, 585-591 (1980), and in Murphy & Webster, op. cit. It is known, in particular, that human influenza **virus** type A includes H1N1, H2N2 and H3N2 subtypes.

SUMM In the composition of the invention, the first and second constituents, that is the conventional **vaccine** and the additive, may be put together in the same container. They may also be present in separate containers placed. . .

SUMM The two constituents of the **vaccine** composition of the invention, whether together or separate, may also be presented in freeze-dried form. The liquid composition is then. . .

SUMM The composition of the invention is generally presented in the form of individual **vaccine** doses (unit doses), constituted either by a **vaccinating**-unit dose of the two constituents mixed, or by a unit dose of conventional **vaccine** and a unit dose of core or fraction of core.

SUMM . . . of the composition of the invention (core) may be obtained according to known methods, particularly by treatment of the influenza **virus** using a protease such as bromelain. This treatment allows the envelope proteins to be separated from the core particles; see. . .

SUMM The second constituent of the **vaccine** composition of the invention may also be composed of an active fraction of influenza **virus** core, this fraction being a protein or lipoprotein fraction, containing at least one active core protein (particularly M protein), or. . . fraction", designate a protein or fragment of protein or core fraction capable of participating in the protection induced by the **vaccine**, like the core particles themselves. The active fragments may be determined by simple routine experiments, retaining those fragments which, associated with the first constituent of the **vaccine** composition, give better protection than that obtained with the first constituent (conventional **vaccine**) alone.

SUMM The core fractions, including a core protein or the fragments of the said protein, may be prepared either by **virus** culture and extraction, or by genetic engineering methods, or by peptidic synthesis, according to methods known per se. it should. . .

SUMM The second constituent (additive) of the **vaccine** of the invention is particularly M protein, or membrane protein, sometimes called matrix protein. Two matrix proteins play a role in the assembly of the **virus** when it replicates: M1 protein, which belongs to the **virus** structure, and M2 protein, which has been detected in the complete **virus** but a considerable proportion of which is not integrated into the mature **virus**. In the present patent application, the expression "M protein" designates the matrix protein found major in the complex **virus**, that is to say M1 protein, which may or may not be mixed with other proteins or core fractions.

SUMM M protein, which may constitute the additive to the **vaccine** according to the invention, may be prepared according to known techniques of protein separation and purification; for example, a method. . .

SUMM treating a core suspension with a **surfactant**, for example a nonionic **surfactant**, at a sufficiently high concentration and at a sufficiently acid pH to favour separation of proteins M and NP in.



SUMM concentrating the supernatant if desired, in order to obtain a core fraction solution constituting an additive for a **vaccine** composition according to the invention.

SUMM The nonionic **surfactant** used is for example a polyoxyethylenated alkyl-phenol- such as Triton X 100 (Rohm & Haas), a polyoxyethylenated fatty alcohol such.

SUMM . . . in order for the additive to be present in effective amount in a volume compatible with its administration as a **vaccine**. If necessary, the **detergent** may be eliminated, for example by dialysis.

SUMM The resulting, possibly concentrated supernatant may be used as an additive, in sufficient quantity to obtain an improvement in the **vaccination**. The quantity of this additive may be assessed for example by reference to the quantity of M protein contained therein.

SUMM The core fractions may also be lipid-free core fractions which may be obtained by gentle treatment of the **virus** by at least one **surfactant**, generally used at weak concentration, for example nonionic **surfactants** such as those commercialized under the name NONIDET P40 or TRITON X100, or certain cationic **surfactants** such as hexadecyl trimethyl ammonium bromide. Suitable concentrations may be determined in each case by routine experiments; they are concentrations.

SUMM When the **vaccine** additive according to the invention is in the form of core particles, these may be core particles obtained through the.

SUMM The **vaccine** composition of the invention may be administered to humans or animals likely to suffer from influenza, notably equine, swine and avian species. The doses of the composition to be administered are the usual ones for this type of **vaccine**, and may if necessary to determined for animals in each case by routine experiments.

SUMM For example, in humans, the unit doses for the first constituent (conventional **vaccine**) are generally defined by their content of hemagglutinin. For each of the three types of **vaccine** ( **vaccine** with complete virion, sub-unit **vaccine** and split **vaccine**) they generally correspond to 1-20 .mu.g, and particularly 5-20 .mu.g, for example 10-15 .mu.g of hemagglutinin of each of the.

SUMM The quantity of additive, in the **vaccine** composition of the invention, is a predetermined quantity sufficient to cause a statistically significant improvement in the efficiency of the **vaccination** in the animal species concerned.

SUMM The quantity of additive to be used with a unit dose of **vaccine** is for example a quantity sufficient to cause a statistical improvement of at least 5%, particularly at least 10%, in **vaccination** efficiency, assessed over at least one recognised criterion of **vaccination** efficiency. The efficiency of the **vaccination** may be determined for example by epidemiological studies of a population **vaccinated** with a conventional **vaccine**, a population **vaccinated** with the conventional **vaccine** and the additive, and possibly a non-**vaccinated** population. The criteria chosen for assessment of **vaccination** efficiency are those commonly used by those specialized in this field and particularly:

SUMM the proportion of **vaccinated** individuals suffering from an influenza affection, compared to the total number of individuals **vaccinated**, in a region where an influenza epidemic has indeed develop;

SUMM or protection against a **virus** subtype other than the subtype(s) used in the preparation of the components (conventional **vaccine** and additive) of the **vaccine**,

SUMM or else the improvement of the effectiveness of the **vaccine** may be evaluated through a statistically significant enhancement of the immune response, as assessed by the percentage of sero-converted subjects, by the amount of antibodies directed against the influenza **virus** or components thereof, or by tests measuring the immunocompetent cell response to the influenza **virus** infection.

SUMM With certain animals species, particularly laboratory animals or with volunteers, it is also possible to determine the efficiency of a **vaccination** by using experimental infection.

SUMM . . . the said quantity of core particles, or else a quantity of the said fraction having the same activity in the **vaccine** composition as the said quantity of core particles).

SUMM When the additive is at least one M protein, or a core fraction containing M protein, the unit dose of **vaccine** composition preferably contains at least 3-5 .mu.g, and particularly at least 7-10 .mu.g of added M protein (that is to say in addition to the free M protein possibly already present in the conventional **vaccine**, notably when it is a split **vaccine**). The quantities of M protein indicated are assessed notably by an immunological test according to the ELISA technique. The amounts. . . quantified, e.g. with bicinchonic acid. One may also proceed by comparison with the M protein content of a purified influenza **virus**, subjected to a **detergent** treatment, by assuming that the M protein represents 50% by weight of the total proteins in the **virus**. The ELISA tests are carried out on tested preparations or on control preparations of M protein of **virus**, in a solution containing for example 0.1% sodium dodecyl sulfate (SDS). The total proteins are dosed for example by any. . .

SUMM It is known that **vaccines** with complete virions, and sub-unit **vaccines** are virtually free from free M protein (that is to say, outside the core or **virus** particles). Conventional split **vaccines** contain certain quantities of M protein, these quantities being variable and depending mainly on the preparation technique used.

SUMM Thus, it is easy to determine the quantities of M protein which have been added to a given **vaccine** composition, by knowledge of the preparation technique used, and thus of the quantities of free M protein normally present in the **vaccine** composition obtained by the said technique.

SUMM . . . measured e.g. in saccharose gradient) which is generally different from that of the M protein already present in the split **vaccine** composition.

SUMM It may be administered in association with other **vaccines** and/or additives.

SUMM The composition may also be used for booster injections, for example 1 to 3 months after the first **vaccination**.

SUMM Another object of the invention is the use of an additive constituted by core of at least one influenza **virus** or by a fraction of core of at least one influenza **virus**, in the preparation of a **vaccine** composition against influenza comprising a conventional influenza **vaccine**.

SUMM . . . particularly concerns use of a second constituent (additive) containing core, or a purified core fraction, of at least one influenza **virus**, in the preparation of a **vaccine** composition against influenza containing a first constituent corresponding to a conventional influenza **vaccine**, it being possible for the said first and second constituents to be present in one and the same container, or. . .

DRWD FIG. 2 shows a comparison of influenza **vaccine** profiles (one dose) before (a) and after (b) addition of 10 .mu.g viral core (FIG. 2 is comprised of six graphs: graph 1a, FIG. 2.1a shows **vaccine** profile before addition of **vaccine** core, with **vaccine** being complete virions; graph 1b, FIG. 2.1b shows **vaccine** profile after addition of **vaccine** core, with **vaccine** being complete virions; graphs 2a and 3a, FIGS. 2.2a and 2.3a show **vaccine** profile before addition of **vaccine** core, with **vaccines** being split **vaccines**; and graphs 2b and 2b, FIGS. 2.2b and 2.3b show **vaccine** profile after addition of **vaccine** core, with the **vaccines** being split **vaccines**).

DETD Obtaining Purified Viral Core

DETD The reassortant strain of influenza **virus** NIB16 (A/H1N1) was used: said strain originates from mating wild strains A/Taiwan/1/86 (A/H1N1) and reassortant X31 (A/H3N2), the latter being obtained by mating strain A/Alchi/2/68 with the A/Porto-Rico/8/34 (A/H1N1) **virus**.

DETD The viral suspensions were prepared by multiplication on chick embryonated eggs, concentration by ultrafiltration and purification on saccharose gradient as described in. . .

DETD To extract the core, the purified **virus**, suspended in phosphate buffer pH 7.4 (PBS buffer), is subjected to two or three successive treatments with bromelain (Sigma) at. . . in 0.1M tris buffer pH 7.5, 1 mM EDTA, 50 mM beta-mercaptoethanol. For the first treatment with the protease, the **viral** suspension, adjusted to contain 2 mg of proteins per ml of buffer solution, is used, and 1 mg/ml of bromelain is added. After 2 hours' incubation at 37.degree. C. and dilution with an **aqueous** solution of 0.1M NaCl, the preparation is subjected to separation by ultra-centrifugation at 120,000 g, for 90 min, at +4.degree. C.. . .

DETD . . . 20-60% (w/w) linear saccharose gradient in PBS buffer at 100,000 g, for 16 hours, at +4.degree. C. The fractions containing **viral** core are diluted by one third with PBS buffer, then subjected to ultra-centrifugation at 120,000 g for 90 minutes, at. . .

DETD hemagglutinating activity is less than 0.01% that of the original **virus** (measurement by hemagglutination according to the method described by Palmer et al., Advanced Laboratory Technicals for Immunological Diagnostic, U.S. Dept.. . .

DETD the final **vaccine** is prepared by diluting in PBS buffer, as indicated in example 2 below.

DETD Preparation of the **Vaccine** and Pharmacological Study

DETD As first constituent of the **vaccine** composition an inactivated monovalent split **vaccine**, obtained with the NIB16 strain, was used.

DETD This split **vaccine** was obtained by treating the **virus** with the mixture of Polysorbate 80 and ether, according to the method described in French patent 2 201 079 (example. . .

DETD The monovalent **vaccine** and the core were diluted and mixed in PBS buffer to provide the combinations and doses indicated in tables 1.

DETD The doses of split **vaccine** and core used are expressed in .mu.g of total proteins determined by colorimetry, by comparison with a standard solution of. . .

DETD One month after **vaccination**, the mice were infected with the A/Wilson Smith/33 (A/H1N1) strain, obtained from the World Influenza Centre in London. This strain. . .

DETD . . . groups were recorded in tables 1 and 2. In the experiments in table 1, no control mouse (unvaccinated) survived. The **viral** core administered alone had at best a limited protective effect (10-20%), and the split **vaccine** injected alone only protected 30 to 50% of the mice. It may be seen that several of the split and core **vaccine** combinations gave synergic protection at concentrations higher than 3 .mu.g of split **vaccine** associated with 90 .mu.g of core, or else, 10 .mu.g of split **vaccine** associated with 10 .mu.g of core.

DETD The increased survival obtained by associating split **vaccine** and core is statically significant. The results were subjected to variance analysis (FISCHER-SNEDECOR test F), which showed that the addition of core has a statistically significant synergic effect (p=0.027) on survival of the **vaccinated** mice.

DETD The experiment was repeated, reducing the range of core quantities tested in associated with the split **vaccine**. The results are presented in table 2. From the results in table 2, it may be seen that the addition of 3 .mu.g of core or more to the **vaccine** systematically increases the percentage of mice surviving the test (highly significant protection synergy: p test F=0.009).

DETD TABLE 1

Surviving mice/Tested mice after immunisation, with, per mouse:				
Split	with added core (.mu.g):			
<b>Vaccine</b> (.mu.g)	0	10	30	90
0 (only PBS)	0/10	1/10	2/10	2/10
3	3/10	2/10	3/10	8/10
10	4/10	7/9	10/10.	. . .

DETD TABLE 2

Surviving mice/Tested mice

after immunisation, with, per mouse:

Split with added core (.mu.g):

Vaccine (.mu.g)			
	0	3	10
0 (only PBS)			
	0/10	0/10	1/10
3	2/10	8/10	10/10
10	6/10	10/10	10/10

- DETD Detection and Quantification of the Influenza **Virus** Core
- DETD The influenza **vaccines** of the invention are likely to contain lipid-free or complete influenza core particles and complete virions or protein sub-units in.
- DETD . . . gradient. In the present case, 14 ml tubes with a 12 ml 20-60% gradient (w/w in PBS) were used. The **vaccine** dose placed in the tubes was 1 ml in volume.
- DETD . . . Edition, Ed. R. C. Weast, GRC Press Inc.) give the apparent density of the particles. Characteristically, the density of the **viral** core (obtained according to the procedure of example 1) is 1.15-1.16 g/cm.sup.3 and that of the **virus** is 1.19-1.20 g/cm.sup.3, this corresponds to saccharose concentrations of 35-37% and 42-44% respectively.
- DETD In order to confirm that the peak observed for a saccharose concentration of 35-37% is **viral** core, polyacrylamide gel electrophoresis (Laemmli, see above) may be used, after denaturing treatment of the sample by SDS at 2%.
- DETD In FIG. 2, the diagrams obtained with 3 different **vaccines** are shown: a **vaccine** with complete virions, commercialized under the trade name **Vaccin** Grippal Ronchese (VGR), and two split **vaccines** obtained with different techniques and commercialized under the trade names VAXIGRIP and MUTAGRIP, these diagrams being established according to the . . . same principles and in the same recording conditions as those described concerning FIG. 1. FIG. 2 allows comparison of influenza **vaccine** profiles (one dose) before (a) and after (b) addition of 10 .mu.g of **viral** core. In FIG. 2, graph 1 corresponds to the **vaccine** with complete virions, and graphs 2 and 3 to the split **vaccines** (Vaxigrip and Mutagrip respectively). The profiles vary from one **vaccine** to another but none of them have a content of core.
- DETD Preparation of a Core Fraction Containing a Matrix Protein (M Protein); **Vaccination** and Dosage Tests
- DETD This fraction is extracted from purified **viral** core according to a technique adapted from Ruigrok and coll. (1989). The core is suspended in PBS buffer adjusted to . . . acetate buffer) may be added, to avoid later degradation of the M protein. The core is then subjected to a **detergent** treatment by a 10% solution of lubrol (Brij 36T, Sigma) the final concentrations of core, lubrol and where necessary TLCK.
- DETD . . . Sparrman et al., (1988). It consisted in capturing the M protein in the samples to be dosed (for example: influenza **virus**, **vaccine**, core, purified proteins) using specific anti-M immunoglobulins adsorbed on microtitration plates; the presence of the M protein was then assessed using a succession of stages which led to a colorimetric reaction proportional to the quantity of **antigen** present.
- DETD Total anti-influenza **virus** M protein immunoglobulins: these specific immunoglobulins were obtained from serum from rabbits hyperimmunized by 3 injections respectively of 100, 75. . . .mu.g of M protein prepared as previously described; these injections were made intra-muscularly at monthly intervals in presence of Freund's **adjuvant** (complete **adjuvant** for the first injection and incomplete for the subsequent ones). The total immunoglobulins were then precipitated with ammonium sulphate at.
- DETD Groups of six-week-old BALB/c mice (from IFFA-Credo, France) were immunized with preparations of Vaxigrip (monovalent A/H1N1 NIB16), with **viral** protein M, or by associations of Vaxigrip and M protein (see doses used in the result tables). The various preparations were administered subcutaneously under 0.5 ml without **adjuvant** and

in a single injection. The mice were tested 4 to 5 weeks after immunization with 5 50% lethal doses. . . .

DETD The two tables presented correspond to two series of experiments carried out with the same M and NIB16 virus core protein preparations. They show that the association of Vaxigrip (monovalent NIB16) and matrix protein preparation improves the protection.

DETD The doses of vaccine, core and protein are expressed in .mu.g of total proteins determined for the vaccine and the core by Bradford's technique (1976, op. cit. in patent), and for M protein by dosage with bicinchonic acid. . . .

DETD TABLE 3

No of surviving mice/No of tested mice  
(10 unless otherwise stated)

	Vaccine NIB16 (.mu.g)	NIB16 M protein (.mu.g)
	0	5 15
0	0	1/9 1
10	0	7 7/9

DETD TABLE 4

No of surviving mice/10 tested mice  
NIB16 vaccine NB16 M protein  
(.mu.g) 0 5 .mu.g

0	1	0
10	2	9

DETD The mice may also be immunized using vaccine preparations with complete virions. The table below presents survival of BALB/c mice immunized at age 6 weeks with trivalent VGR vaccine preparations with complete virions (Vaccin Grippal Ronchese from the 1990-91 season). The trivalent vaccine dose used was about 5 .mu.g hemagglutinine of NIB16 virus per mouse; it was quantified by radial immunodiffusion according to the technique of Wood & coll., op. cit., and corresponds. . . .

DETD . . . show that the improvement effect in protection by addition of M protein preparation may also be observed with a complete virus vaccine:

DETD TABLE 5

No of surviving mice/10 mice tested	Complete virion	VGR vaccine M Protein NIB16 (.mu.g)	(.mu.g HA NIB16)
		0	5 15
0	0	0	0
5	2	4	7

DETD In the same way as before, the BALB/c mice were immunized using sub-unit vaccine preparations, such as the DUPHAR vaccine (Influvac sub-unit); this is obtained after treatment of the virus by hexadecyl trimethyl ammonium bromide (Jennings, Smith et al, 1984; Bachmayer, 1975) and purification of the HA and NA glycoproteins. . . .

DETD This sub-unit vaccine may be associated with core particles or a core fraction containing M protein using equivalent doses to those in the previous tests, i.e. for the monovalent or trivalent vaccine : the equivalent of 5 .mu.g of HA of virus NIB16 assessed by radial immunodiffusion; for the M protein: 5, 15 or 30 .mu.g of protein dosed by the bicinchonic. . . .

DETD Bachmayer, H. (1975). "Selective solubilization of hemagglutinin and neuraminidase from influenza viruses." Intervirology, 5, 260-272.

DETD Bucher, D. J., Kharitononkov, I. G., Wajeed-Khan, M., Palo, A., Holloway, D. and Mikhail, A. (1987). "Detection of influenza viruses through selective adsorption and detection of the M

- protein antigen." J. of Immunol. Methods, 96, 77-85.
- DETD Jennings, R., Smith, T. L., Spencer, R. C., Mellersh, A. M., Edey, D., Fenton, P., et al (1984). "Inactivated influenza **virus vaccines** in man: a comparative study of subunit and split **vaccines** using two methods for assessment of antibody responses." **Vaccine**, 2, 75-080.
- DETD Ruigrok, R. W. H., Calder, L. J. and Wharton, S. T. A. (1989). "Electron Microscopy of the Influenza **Virus** Submembranal Structure." Virology, 173, 311-316.
- DETD Improvement of Protection against a Sub Type of the Influenza **Virus** by use of a Different Sub-Type **vaccine** Containing Core
- DETD Groups of OF1 male mice aged 6 weeks were treated with preparations of monovalent Vaxigrip A/H3N2.times.97, A/H3N2.times.97 **virus** core, or with associations of Vaxigrip and core. The different preparations were administered subcutaneously under a volume of 0.5 ml, without **adjuvants** and in a single injection. The mice were tested 5 weeks after immunization with a dose corresponding to 20 50%.

DETD TABLE 6

No surviving mice/no tested mice (10 unless otherwise stated)

Vaccine X97 (.mu.g)	core X97 added (.mu.g)			
	0	3	10	30
0	0/9	0/9	0	0
8	0	0	0	0/9
10	1	3	3	1
30.				

- DETD as expected, **vaccine** A/H3N2 X97 does not afford protection against an infection challenge with **virus** A/H1N1. A surprising effect of protection synergy is observed however when the **vaccine** is associated with core.
- CLM What is claimed is:
1. In a **vaccine** composition which comprises an anti-influenza **vaccine** selected from the group consisting of a complete virion **vaccine**, a sub-unit **vaccine**, and a split **vaccine**, wherein the improvement comprises having an additive selected from the group consisting of: M protein from at least one influenza **virus** strain; an isolated influenza **virus** core particle including M protein from at least one influenza **virus** strain; and an isolated portion, including M protein, of an influenza **virus** core particle, from at least one influenza **virus** strain.
  2. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 1.
  3. A **vaccine** composition according to claim 1, wherein said anti-influenza **vaccine** is a complete virion **vaccine**.
  4. A **vaccine** composition according to claim 1, wherein said anti-influenza **vaccine** is a split **vaccine**.
  5. A **vaccine** composition according to claim 1, wherein said anti-influenza **vaccine** is a sub-unit **vaccine**.
  6. A **vaccine** composition according to claim 1 wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza **vaccine**.
  7. A **vaccine** composition according to claim 6 wherein it contains as the additive at least 3-5 .mu.g of M protein.
  8. A **vaccine** composition according to claim 6 wherein it contains as the additive at least 7-.mu.g of M protein.

9. A **vaccine** composition according to claim 6 wherein its anti-influenza **vaccine** component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
10. The **vaccine** composition of claim 1 wherein the additive comprises isolated M protein.
11. The **vaccine** composition of claim 1 wherein the additive comprises an isolated portion of an influenza **virus** core particle.
12. The **vaccine** composition of claim 1 wherein the additive comprises an isolated influenza **virus** core particle.
13. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 10.
14. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 11.
15. A method for inducing an immunological response in a host comprising inoculating the host with the **vaccine** composition of claim 12.
16. A **vaccine** composition according to claim 10, wherein said anti-influenza **vaccine** is a split **vaccine**.
17. A **vaccine** composition according to claim 10, wherein said anti-influenza **vaccine** is a sub-unit **vaccine**.
18. A **vaccine** composition according to claim 10, wherein said anti-influenza **vaccine** is a complete virion **vaccine**.
19. A **vaccine** composition according to claim 11, wherein said anti-influenza **vaccine** is a split **vaccine**.
20. A **vaccine** composition according to claim 11, wherein said anti-influenza **vaccine** is a sub-unit **vaccine**.
21. A **vaccine** composition according to claim 11, wherein said anti-influenza **vaccine** is a complete virion **vaccine**.
22. A **vaccine** composition according to claim 12, wherein said anti-influenza **vaccine** is a split **vaccine**.
23. A **vaccine** composition according to claim 12, wherein said anti-influenza **vaccine** is a sub-unit **vaccine**.
24. A **vaccine** composition according to claim 12, wherein said anti-influenza **vaccine** is a complete virion **vaccine**.
25. A **vaccine** according to claim 10, wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza **vaccine**.
26. A **vaccine** according to claim 11, wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza **vaccine**.
27. A **vaccine** according to claim 12, wherein it is presented in the form of a unit dose containing an immunologically effective amount of the additive sufficient to effect enhancement of the anti-influenza **vaccine**.
28. A **vaccine** composition according to claim 25 wherein it contains as the additive at least 3-5 .mu.g of M protein.
29. A **vaccine** composition according to claim 26 wherein it contains as the additive at least 3-5 .mu.g of M protein.

30. A **vaccine** composition according to claim 27 wherein it contains as the additive at least 3-5 .mu.g of M protein.
31. A **vaccine** composition according to claim 25 wherein it contains as the additive at least 7-10 .mu.g of M protein.
32. A **vaccine** composition according to claim 26 wherein it contains as the additive at least 7-10 .mu.g of M protein.
33. A **vaccine** composition according to claim 27 wherein it contains as the additive at least 7-10 .mu.g of M protein.
34. A **vaccine** composition according to claim 25 wherein its anti-influenza **vaccine** component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
35. A **vaccine** composition according to claim 26 wherein its anti-influenza **vaccine** component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
36. A **vaccine** composition according to claim 27 wherein its anti-influenza **vaccine** component contains from 1 to 20 .mu.g of hemagglutinin of each of the strains of which it is composed.
37. An anti-influenza **vaccine** kit comprising as a first component at least one anti-influenza **vaccine** selected from the group consisting of a complete virion **vaccine**, a sub-unit **vaccine**, and a split **vaccine**, and, a second component selected from the group consisting of: M protein from at least one influenza **virus** strain; an isolated influenza **virus** core particle including M protein from at least one influenza **virus** strain; and an isolated portion, including M protein, of an influenza **virus** core particle, from at least one influenza **virus** strain.
38. The **vaccine** kit according to claim 37, wherein said first component and the second component are present in the same container.
39. The **vaccine** kit according to claim 37, wherein said first component and the second component are present in separate containers, placed in. . .
41. The kit of claim 37 wherein the second component comprises an isolated portion of an influenza **virus** core particle.
42. The kit of claim 37 wherein the second component comprises an isolated influenza **virus** core particle.
43. A **vaccine** kit according to claim 40, wherein said first component and the second component are present in the same container.
44. A **vaccine** kit according to claim 40, wherein said first component and the second component are present in separate containers, placed in. . .
45. A **vaccine** kit according to claim 41, wherein said first component and the second component are present in the same container.
46. A **vaccine** kit according to claim 41, wherein said first component and the second component are present in separate container, placed in. . .
47. A **vaccine** kit according to claim 42, wherein said first component and the second component are present in the same container.
48. A **vaccine** kit according to claim 42, wherein said first component and the second component are present in separate containers, placed in. . .
49. In a **vaccine** composition which comprises an anti-influenza **vaccine** selected from the group consisting of a complete virion **vaccine**, a sub-unit **vaccine**, and a split **vaccine**, wherein the improvement comprises having an additive



which includes M protein from at least one influenza **virus** strain wherein the additive is obtained by a process consisting essentially of: treating a core suspension with a **surfactant**, at a sufficiently high concentration and at a sufficiently acid pH to favor separation of proteins M and NP in. . .

50. The **vaccine** composition of claim 49 wherein the process for obtaining the additive further comprises concentrating the supernatant.

51. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 49.

52. A **vaccine** composition according to claim 49 wherein the **surfactant** is a nonionic **surfactant**.

53. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 50.

54. The **vaccine** of claim 52 wherein the nonionic **surfactant** is selected from the group consisting of polyoxyethylenated alkylphenols, polyxyethylenated fatty alcohols and alkyl-osides.

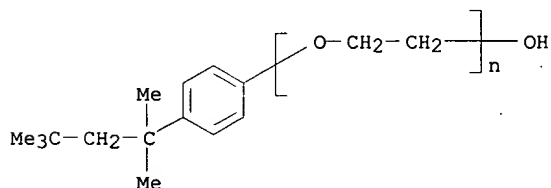
55. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 54.

56. A method for inducing an immunological response in a host comprising inoculating said host with the **vaccine** composition according to claim 52.

IT 9002-92-0  
(in M protein sepn. for influenza vaccine component)

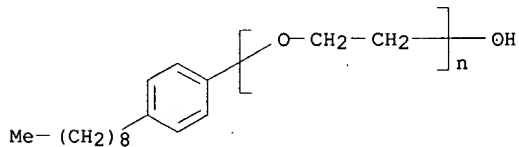
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 TI **Detergent**-facilitated immunoassay for the rapid and quantitative assay of pharmacological agents  
 IN Cheng, Anthony K., Anaheim, CA, United States  
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 AI US 1994-283116 19940729 (8)  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Green, Lora M.; Assistant Examiner: Wolski, Susan C.  
 LREP May, William H., Hampson, Gary T.  
 CLMN Number of Claims: 28  
 ECL Exemplary Claim: 1  
 DRWN 1 Drawing Figure(s); 1 Drawing Page(s)  
 LN.CNT 1403  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Methods for modulating the rates and dose responses of immunoassays through the incorporation of one or more **detergents** into the immunoassay reaction are disclosed. The methods are particularly suitable for automated immunoassay formats, especially with formats that use analyte-biotin bidentate reagents. The methods may be used to facilitate the detection of any desired, preselected pharmacological agent.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 9002-93-1, Triton X-100  
 (detergent-facilitated immunoassay of drugs)  
 RN 9002-93-1 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 20

L74 ANSWER 20 OF 28 USPATFULL  
 AN 97:5959 USPATFULL  
 TI Contraceptive compositions  
 IN Brode, George L., Bridgewater, NJ, United States  
 Doncel, Gustavo F., Norfolk, VA, United States  
 Gabelnick, Henry L., N. Bethesda, MD, United States  
 Kreeger, Russell L., Flemington, NJ, United States  
 Salensky, George A., White House Station, NJ, United States  
 PA Medical College of Hampton Roads, Arlington, VA, United States (U.S.  
 corporation)  
 Biomaterials Corporation, Plainsboro, NJ, United States (U.S.  
 corporation)  
 PI US 5595980 19970121  
 AI US 1995-418884 19950407 (8)  
 RLI Continuation of Ser. No. US 1993-129253, filed on 29 Sep 1993, now  
 abandoned  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Wityshyn, Michael G.; Assistant Examiner: Prats,  
 Francisco C.  
 LREP Banner & Witcoff Ltd.  
 CLMN Number of Claims: 8  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 859  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB Improved contraceptive compositions are disclosed which comprise a  
 spermicide or virucide, a polymeric delivery component and optionally a  
 cosmetic ingredient. The improvement is directed to the use of certain  
 hydrophobically modified polysaccharides as the polymeric delivery  
 component. Quite advantageously, the hydrophobically modified  
 polysaccharides of the present invention can alter sperm motility.  
 Moreover, the hydrophobically modified polysaccharides can provide  
 reduced irritation potential when used in combination with spermicides  
 such as, for example, nonoxynol-9, which may reduce the potential for  
 infection of sexually transmitted diseases such as HIV and herpes.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 26027-38-3, Nonoxynol-9  
 (contraceptive comps.)  
 RN 26027-38-3 USPATFULL  
 CN Poly(oxy-1,2-ethanediyl), .alpha.-(4-nonylphenyl)-.omega.-hydroxy- (9CI)  
 (CA INDEX NAME)



=&gt; d kwic 20

L74 ANSWER 20 OF 28 USPATFULL  
 SUMM . . . such increased risks of vaginal irritation, there may be  
 increased risks of contracting sexually transmitted diseases of  
 bacterial, fungal or viral origin, such as, for example, HIV  
 and herpes.  
 DETD . . . 500 centipoise. Unless otherwise indicated, as used herein the  
 term "viscosity" refers to the viscosity of a 2.0 weight percent  
 aqueous solution of the polymer measured at 25.degree.  
 C. with a Brookfield viscometer. Such viscosity measuring techniques are

known to those skilled. . . .

DETD . . . are known to those skilled in the art and are often referred to in the art as diluents, solvents and **adjuvants**. Typically cosmetic ingredients include, for example; water, ethyl alcohol, isopropyl alcohol, glycerin, glycerol propylene glycol, sorbitol and other high molecular. . . . 0.1 to 5% weight based on the weight of the contraceptive compositions, of other additives, such as, for example; stabilizers, **surfactants**, menthol, eucalyptus oil, other essential oils, fragrances, and the like. Polyoxyethylene 20osorbitan monolaurate is a preferred stabilizer for use in. . . .

DETD . . . sodium hydroxide solution containing 20 wt % sodium hydroxide was added. After stirring for 30 minutes, 64 g of an **aqueous solution** containing 40 wt % HSl was added. The reactor mixture was heated to 55.degree. C. and held there for 2 hours. Then 8.7 grams of an **aqueous solution** containing 70 wt % CS1 was added. The mixture was held at 55.degree. C. for another hour. The reaction was. . . with 3 grams glacial acetic acid. The reaction slurry was filtered and washed 7 times with 400 grams of an **aqueous solution** containing 90 wt % acetone, once with 400 grams of an **aqueous solution** containing 94 wt % acetone, and once with 400 grams of a solution containing 0.5 milliliter of a 40 wt. . . .

DETD One hundred gram **aqueous solutions** containing 1.5 weight percent of the polymeric delivery component being tested were prepared. To each solution, 4.16 grams of N-9. . . .

DETD A contraceptive gel was prepared by mixing 2.5 g of a 2.5 wt % **aqueous solution** of POL. 2 with 2.5 g of 3 wt % solution of POL. 3 and 0.2 g of N-9. A. . . .

DETD A contraceptive lotion was prepared by combining 62.5 grams of an **aqueous solution** containing 10 wt. % CL, 104.2 grams of an **aqueous solution** containing 6 wt. % POL. 1, 25.0 grams of P-20 and 808.3 grams of water. The resulting lotion contained 0.625. . . .

IT 3001-63-6, Quab 426 9003-39-8, PVP 9004-62-0, Hydroxyethyl cellulose .  
 9004-64-2, Hydroxypropyl cellulose 9036-19-5, Octoxynol-9  
 26027-38-3, Nonoxynol-9 29756-57-8, Nonylphenyl glycidyl ether  
 50744-78-0, Quab 342  
 (contraceptive compns.) .

=&gt; d bib abs hitstr 21

L74 ANSWER 21 OF 28 USPATFULL  
 AN 90:11136 USPATFULL  
 TI Process for preparing immunogenic complexes and pharmaceutical composition containing these complexes  
 IN De Vries, Petra, Almere, Netherlands  
 van Wezel, deceased, Antonius L., late of Bilthoven, Netherlands by Cornelia M. van Wezel-Berendse, administratrix  
 Beuvery, Eduard C., Vianen, Netherlands  
 PA De Staat der Nederlanden Vertegenwoordigd door de Minister van Welzijn, Volksgezondheid en Cultuur, Leidschendam, Netherlands (non-U.S. corporation)  
 PI US 4900549 19900213  
 AI US 1987-3070 19870114 (7)  
 PRAI NL 1986-66 19860114  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Moskowitz, Margaret; Assistant Examiner: Kushan, Jeff  
 LREP Brumbaugh, Graves, Donohue & Raymond  
 CLMN Number of Claims: 15  
 ECL Exemplary Claim: 1  
 DRWN 10 Drawing Figure(s); 5 Drawing Page(s)  
 LN.CNT 419

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a process for preparing immunogenic complexes in which an amphiphatic **antigenic** protein or peptide in dissolved or solubilized form is contacted with a solution containing a **detergent**, a sterol, and a glycoside comprising hydrophobic and hydrophilic regions, in at least the critical **micelle** forming concentration, the **detergent** is removed, and the immunogenic complex formed is purified. Optionally, the solution with which the **antigenic** protein or peptide is contacted also contains a phospholipid, preferably phosphatidylethanolamine. The preferred sterol is cholesterol, and preferred glycosides are saponins, especially Quil A.

The immunogenic complex is useful as a **vaccine**. Its immunogenic power is higher than that of corresponding **micelles** formed by aggregation of the **antigens**, and is also higher than that of the **antigens** incorporated in liposomes.

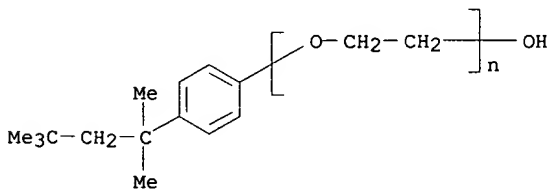
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 9002-93-1, Triton X-100

(immunogenic complex-contg. micelles for vaccines formation with)

RN 9002-93-1 USPATFULL

CN Poly(oxy-1,2-ethanediyl), .alpha.-[4-(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 22

L74 ANSWER 22 OF 28 USPATFULL  
 AN 88:13242 USPATFULL  
 TI Aryl and heteroaryl ethers as agents for the treatment of hypersensitive ailments  
 IN Chakraborty, Utpal R., Orangeburg, NY, United States  
 Youssefeyeh, Raymond D., Tarrytown, NY, United States  
 PA USV Pharmaceutical Corporation, Fort Washington, PA, United States (U.S. corporation)  
 PI US 4728668 19880301  
 AI US 1986-877570 19860623 (6)  
 RLI Division of Ser. No. US 1985-723781, filed on 16 Apr 1985, now patented, Pat. No. US 4631287  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Friedman, Stanley J.  
 CLMN Number of Claims: 6  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 551

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is concerned with the therapeutic composition comprising as an active ingredient a compound of the formula:

(R.sub.1)(R.sub.2) Ar--Z--M--Ar.sub.1 (R.sub.3)(R.sub.4) I

and salts thereof;

wherein

Ar and Ar.sub.1 are independently phenyl, naphthyl or a nitrogen, oxygen, or sulfur heterocyclic ring;

Z is an alkylene chain containing from 1 to 5 carbon atoms in the principal chain and up to a total of 10 carbon atoms;

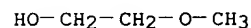
M is oxygen, sulfur, or NR.sub.5 ;

R.sub.1, R.sub.2, R.sub.3 and R.sub.4 are each independently H, lower alkyl, lower alkoxy, hydroxy, halo, trihalomethyl, hydroxy lower alkyl, carboxy, formyl, aryl, aryloxy, benzyloxy, lower alkanoyl, carboxy lower alkoxy, nitro, amino, lower alkylamino, dilower alkylamino, cyano, lower alkanoyloxy, carbamoyl, lower alkoxy-alkoxy, carbo-lower alkoxy-alkoxy, or tetrahydropyranylmethyl; and

R.sub.5 is hydrogen or lower alkyl.

## CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 109-86-4, 2-Methoxyethanol  
 (reaction of, with (chloromethyl)quinoline)  
 RN 109-86-4 USPATFULL  
 CN Ethanol, 2-methoxy- (8CI, 9CI) (CA INDEX NAME)



=&gt; d bib abs hitstr 24

L74 ANSWER 24 OF 28 USPATFULL

AN 87:7997 USPATFULL

TI Plasminogen activator derivatives

IN Shimizu, Kimihiro, Yoshikawa, Japan

Nakahara, Tsuguji, Tokyo, Japan

Kinoshita, Taketoshi, Koshigaya, Japan

Takatsuka, Jun, Kawasaki, Japan

Igarashi, Michiko, Musashino, Japan

PA Nippon Chemiphar Company, Ltd., Tokyo, Japan (non-U.S. corporation)

PI US 4640835 19870203

AI US 1983-546590 19831028 (6)

DCD 20020122

RLI Continuation-in-part of Ser. No. US 1982-437009, filed on 27 Oct 1982, now patented, Pat. No. US 4495285

DT Utility

FS Granted

EXNAM Primary Examiner: Shapiro, Lionel M.

LREP Oblon, Fisher Spivak, McClelland &amp; Maier

CLMN Number of Claims: 24

ECL Exemplary Claim: 1

DRWN 18 Drawing Figure(s); 13 Drawing Page(s)

LN.CNT 1329

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Derivatives of a nonimmunogenic plasminogen activator which comprises at least one polyalkylene glycol group chemically bonded with at least one coupling agent to amino acid side chains of said plasminogen activator, wherein said polyalkylene glycol has a molecular weight of about 200-20,000 and is unsubstituted or is substituted with one or more alkyl, alkoxy or alkanoyl groups or a mixture thereof.

The plasminogen activator derivatives have an extended circulating life in the mammalian bloodstream and also inhibit the formation of thrombus in the same.

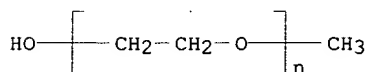
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 9004-74-4 9004-99-3 9005-00-9

(reaction of, with cyanuric acid chloride)

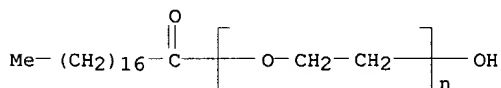
RN 9004-74-4 USPATFULL

CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



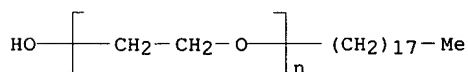
RN 9004-99-3 USPATFULL

CN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI) (CA INDEX NAME)



RN 9005-00-9 USPATFULL

CN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI) (CA INDEX NAME)



CEPERLEY 09/647,518

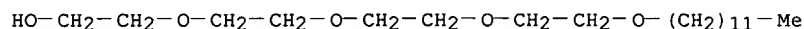


# ds can of some lauryl epds

CEPERLEY 09/647,518

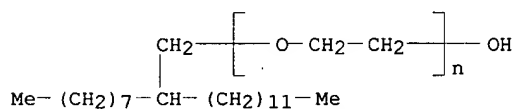
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L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN 3,6,9,12-Tetraoxatetracosan-1-ol (6CI, 7CI, 8CI, 9CI)  
MF C20 H42 O5  
CI COM



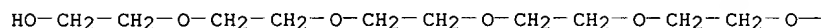
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):22

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Poly(oxy-1,2-ethanediyl), .alpha.-(2-octyltetradecyl)-.omega.-hydroxy-  
(9CI)  
MF (C2 H4 O)<sub>n</sub> C22 H46 O  
CI PMS

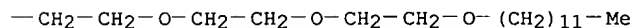


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN 3,6,9,12,15,18,21,24-Octaoxahexatriacontan-1-ol (7CI, 8CI, 9CI)  
MF C28 H58 O9  
CI COM

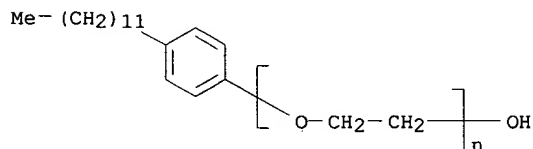
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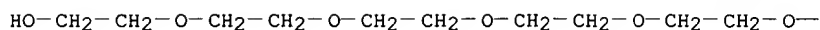


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Poly(oxy-1,2-ethanediyl), .alpha.-(4-dodecylphenyl)-.omega.-hydroxy- (9CI)  
MF (C2 H4 O)<sub>n</sub> C18 H30 O  
CI PMS, COM

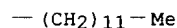


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN 3,6,9,12,15-Pentaoxaheptacosan-1-ol (6CI, 7CI, 8CI, 9CI)  
MF C22 H46 O6  
CI COM

PAGE 1-A

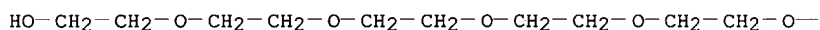


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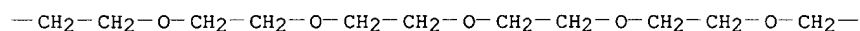


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 41-hydroxy-3,6,9,12,15,18,21,24,27,30,33,36,39-  
 tridecaoxahentetracont-1-yl ester (9CI)  
 MF C40 H80 O16

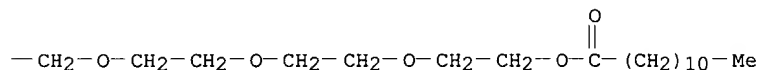
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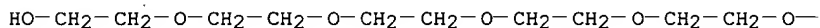


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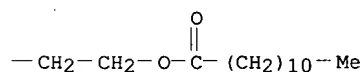


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 17-hydroxy-3,6,9,12,15-pentaoxaheptadec-1-yl ester (9CI)  
 MF C24 H48 O8

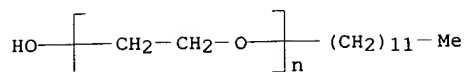
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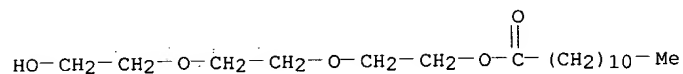
PAGE 1-B



L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Poly(oxy-1,2-ethanediyl), .alpha.-dodecyl-.omega.-hydroxy- (9CI)  
 ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT  
 MF (C2 H4 O)<sub>n</sub> C12 H26 O  
 CI PMS, COM

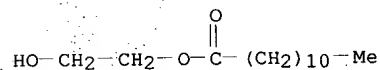


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 2-[2-(2-hydroxymethylethoxy)methylethoxy]methylethyl  
 ester (9CI)  
 MF C21 H42 O5  
 CI IDS



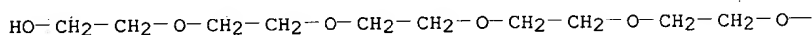
3 ( D1-Me )

L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 2-hydroxyethyl ester (9CI)  
 MF C14 H28 O3

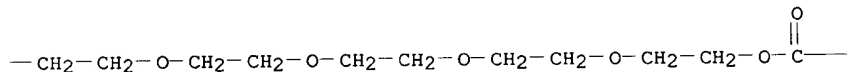


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 29-hydroxy-3,6,9,12,15,18,21,24,27-nonaoxanonacos-1-yl  
 ester (9CI)  
 MF C32 H64 O12  
 CI COM

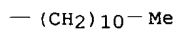
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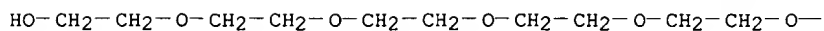


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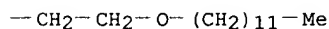


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN 3,6,9,12,15,18-Hexaoxatriacontan-1-ol (6CI, 7CI, 8CI, 9CI)  
 MF C24 H50 O7  
 CI COM

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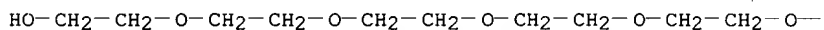


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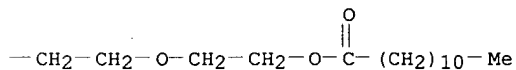


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Dodecanoic acid, 20-hydroxy-3,6,9,12,15,18-hexaoxaicos-1-yl ester (9CI)  
MF C26 H52 O9

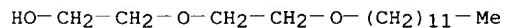
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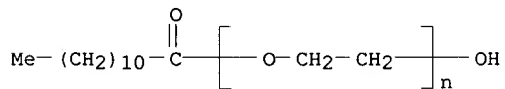
PAGE 1-B



L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Ethanol, 2-[2-(dodecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI)  
MF C16 H34 O3  
CI COM

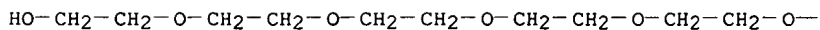


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxododecyl)-.omega.-hydroxy- (9CI)  
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT  
MF (C2 H4 O)<sub>n</sub> C12 H24 O2  
CI PMS, COM

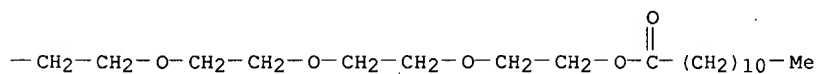


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Dodecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaohexacos-1-yl ester (9CI)  
MF C30 H60 O11

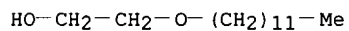
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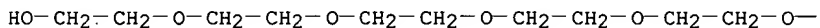


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Ethanol, 2-(dodecyloxy)- (6CI, 7CI, 8CI, 9CI)  
MF C14 H30 O2  
CI COM

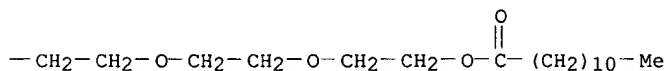


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Dodecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaotricos-1-yl ester (9CI)  
MF C28 H56 O10

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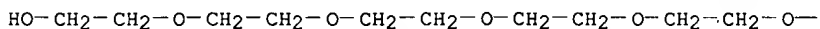


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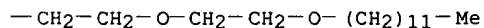


L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN 3,6,9,12,15,18,21-Heptaotritriacontan-1-ol (6CI, 7CI, 8CI, 9CI)  
MF C26 H54 O8  
CI COM

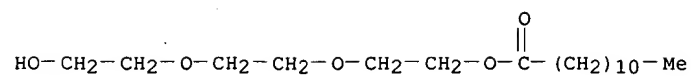
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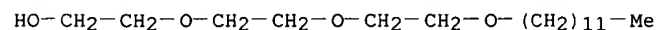
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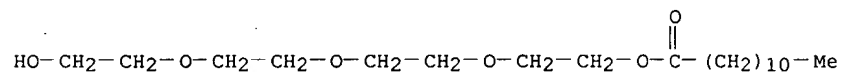
L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Dodecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI)  
MF C18 H36 O5



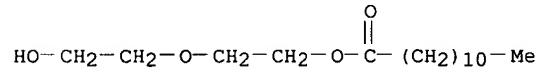
L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Ethanol, 2-[2-[2-(dodecyloxy)ethoxy]ethoxy]- (6CI, 7CI, 8CI, 9CI)  
 MF C18 H38 O4  
 CI COM



L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl ester (9CI)  
 MF C20 H40 O6



L13 23 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Dodecanoic acid, 2-(2-hydroxyethoxy)ethyl ester (9CI)  
 MF C16 H32 O4  
 CI COM



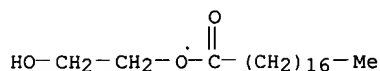
ALL ANSWERS HAVE BEEN SCANNED

disc of some stearate  
cpds

CEPERLEY 09/647,518

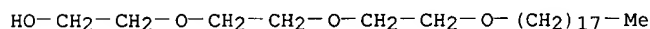
=> d scan

L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, 2-hydroxyethyl ester (9CI)  
MF C20 H40 O3  
CI COM

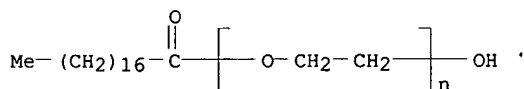


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):18

L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Ethanol, 2-[2-[2-(octadecyloxy)ethoxy]ethoxy]- (6CI, 7CI, 8CI, 9CI)  
MF C24 H50 O4

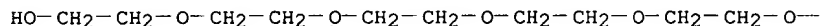


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Poly(oxy-1,2-ethanediyl), .alpha.-(1-oxooctadecyl)-.omega.-hydroxy- (9CI)  
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT  
MF (C2 H4 O)<sub>n</sub> C18 H36 O2  
CI PMS, COM

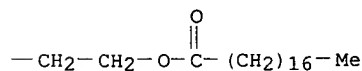


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, 17-hydroxy-3,6,9,12,15-pentaoxaheptadec-1-yl ester (9CI)  
MF C30 H60 O8  
CI COM

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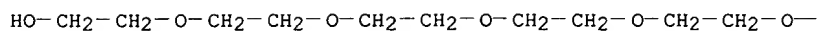


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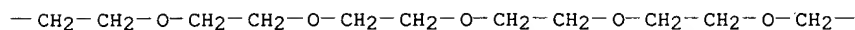


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, 41-hydroxy-3,6,9,12,15,18,21,24,27,30,33,36,39-tridecaoxahentetracont-1-yl ester (9CI)  
MF C46 H92 O16

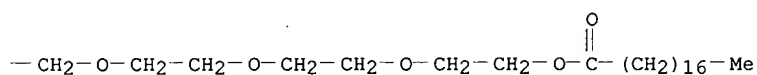
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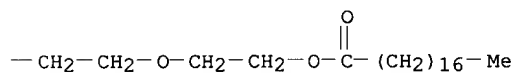


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, 20-hydroxy-3,6,9,12,15,18-hexaoxaicos-1-yl ester (9CI)  
MF C32 H64 O9  
CI COM

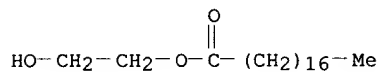
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L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, hydroxy-, 2-hydroxyethyl ester (8CI, 9CI)  
MF C20 H40 O4  
CI IDS

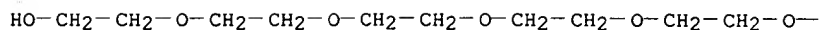


D1-OH

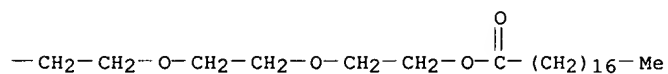
L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
IN Octadecanoic acid, 23-hydroxy-3,6,9,12,15,18,21-heptaotricos-1-yl ester (9CI)  
MF C34 H68 O10



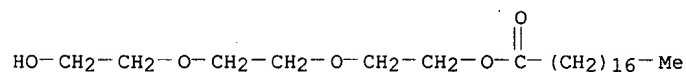
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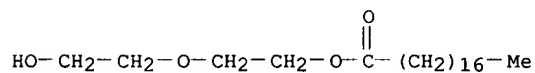


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 2-[2-(2-hydroxymethylethoxy)methylethoxy]methylethyl  
 ester (9CI)  
 MF C27 H54 O5  
 CI IDS

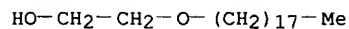


3 ( D1-Me )

L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 2-(2-hydroxyethoxy)ethyl ester (9CI)  
 MF C22 H44 O4  
 CI COM

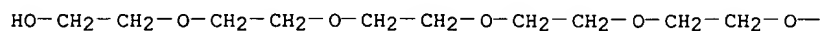


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Ethanol, 2-(octadecyloxy)- (6CI, 7CI, 8CI, 9CI)  
 MF C20 H42 O2  
 CI COM

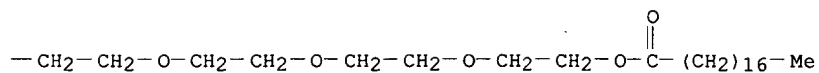


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 26-hydroxy-3,6,9,12,15,18,21,24-octaohexacos-1-yl  
 ester (9CI)  
 MF C36 H72 O11

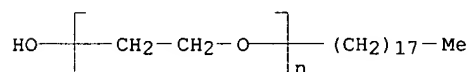
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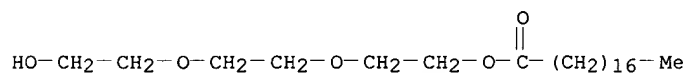
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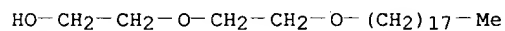
L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Poly(oxy-1,2-ethanediyl), .alpha.-octadecyl-.omega.-hydroxy- (9CI)  
 ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT  
 MF (C2 H4 O)<sub>n</sub> C18 H38 O  
 CI PMS, COM



L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI)  
 MF C24 H48 O5

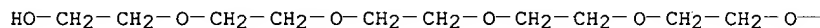


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Ethanol, 2-[2-(octadecyloxy)ethoxy]- (6CI, 7CI, 8CI, 9CI)  
 MF C22 H46 O3  
 CI COM

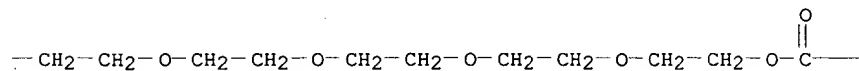


L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 29-hydroxy-3,6,9,12,15,18,21,24,27-nonaoxanonacos-1-yl ester (9CI)  
 MF C38 H76 O12

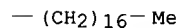
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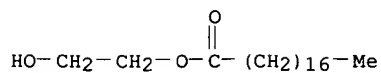
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L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, hydroxy-, monoester with 1,2-propanediol (8CI, 9CI)  
 MF C21 H42 O4  
 CI IDS

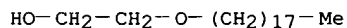


D1-Me

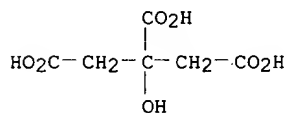
D1-OH

L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, mono[2-(octadecyloxy)ethyl]  
 ester (9CI)  
 MF C26 H48 O8  
 CI IDS

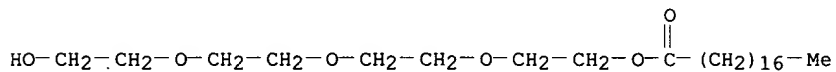
CM 1



CM 2



L14 19 ANSWERS REGISTRY COPYRIGHT 2001 ACS  
 IN Octadecanoic acid, 2-[2-[2-(2-hydroxyethoxy)ethoxy]ethoxy]ethyl ester  
 (9CI)  
 MF C26 H52 O6



ALL ANSWERS HAVE BEEN SCANNED

=> d bib abs hitstr 8

L48 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 1991:519977 HCAPLUS

DN 115:119977

TI Enhancing properties of surfactants on the release of carbamazepine from suppositories

AU Fontan, J. E.; Arnaud, P.; Chaumeil, J. C.

CS Dep. Pharmacotech., Fac. Sci. Pharm. Biol., Paris, 75270, Fr.

SO Int. J. Pharm. (1991), 73(1), 17-21

CODEN: IJPHDE; ISSN: 0378-5173

DT Journal

LA English

AB The effect of surfactants on physicochem. properties and on the release characteristics of carbamazepine from fatty suppositories was investigated in vitro. Four surfactants, polyoxyethylene 50-stearate (Simulsol M), polyoxyethylene 23-lauryl ether (Brij 35), and polysorbates 20 and 80, were examd. as adjuvants. The dissoln. rate was enhanced by all surfactants used. The dissoln. rate at 30 min increased from 54% without surfactant, to 100% with polysorbate 80 (2%). The liquefaction time could be the limiting factor for the dissoln. rate of carbamazepine. The better solubilizing effect of polysorbate 80 can be due to the better incorporation capacity of its micelle.